MAR 6 1924
Medical Lib.

VOLUME 8 NUMBER 2

ARCHIVES OF SURGERY

EDITORIAL BOARD

DEAN LEWIS, Chicago
EVARTS A. GRAHAM, St. Louis THOMAS CULLEN, Baltimore
HUGH CABOT, Ann Arbor, Mich. WILLIAM DARRACH, New York City
EDWARD STARR JUDD, Rochester, Minn.

MARCH, 1924

PUBLISHED BIMONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second-Class Matter, July 14, 1920, at the Postoffice at Chicago, Illinois, Under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of Oct. 3, 1917, authorized July 29, 1920.

CONTENTS OF PREVIOUS NUMBERS

JANUARY, 1924. NUMBER 1—PART I

Arm-Chest Adhesions: Brachiothoracic Adhesions, Axillary Webs. John Staige Davis, M.D., Baltimore.

Mono-Osteitic Type of Paget's Disease of Bone (Osteitis Deformans): Report of Three Cases. Francis C. Newton, M.D., Boston.

Surgery of the Pituitary Body, with Illustrative Cases. Charles H. Frazier, M.D., Philadelphia.

Etiology of Exstrophy of the Bladder. Charles E. von Geldern, M.D., Sacramento, Calif.

Tumors of the Epididymis, Spermatic Cord and Testicular Tunics: A Review of the Literature and Report of Three New Cases. Frank Hinman, M.D., and Thomas E. Gibson, M.D., San Francisco.

A Method of Estimating the Extensiveness of Lesions (Burns and Scalds) Based on Surface Area Proportions. Samuel Gordon Berkow, M.D., Perth Amboy, N. J.

Studies of Exophthalmic Goiter and the Involuntary Nervous System. X. The Course of the Subjective and Objective Manifestations in Fifty Unselected Patients Observed Over a Period of Two Years, in Whom No Specific Therapeutic Measures Were Instituted ("Spontaneous Course"). Harold Thomas Hyman, M.D., and Leo Kessel, M.D., New York.

Arterial Circulation of Thyroid Adenomas. Wallace I. Terry, M.D., and Granville S. Delamere, M.D., San Francisco.

Immediate Effect of Subtotal Thyroidectomy in Toxic Goiter; Daily Basal Metabolism and Pulse Observations. Harold N. Segall, M.D., and James H. Means, M.D., Boston.

Twenty-Second Report of Progress in Orthopedic Surgery. Robert B. Osgood, M.D.; Nathaniel Allison, M.D.; Robert Soutter, M.D.; Harry C. Low, M.D.; Murray S. Danforth, M.D.; C. Herman Bucholz, M.D.; Lloyd T. Brown, M.D.; Philip D. Wilson, M.D., and M. N. Smith-Petersen, M.D., Boston.

Book Review.

JANUARY, 1924. NUMBER 1—PART II

Officers for 1922-1923.

Officers for 1923-1924.

Suppuration in the Posterior Mediastinum, with Report of Cases. William Lerche, M.D., St. Paul.

Value of the Lateral Projection in the Roentgen-Ray Examination of the Chest, with Special Reference to the Surgical Treatment of Abscess of the Lung. Leon T. Le Wald, M.D., and Nathan W. Green, M.D., New York.

Operation for Acute Empyema on Physiologic Lines. Otto C. Pickhardt, M.D., New York.

Malignant Tumor of the Lung: Necessity for Early Operation. Howard Lilienthal, M.D., New York.

Intracardiac Surgery. Duff S. Allen, M.D., St. Louis.

Three Cases Illustrating the Open Method of Intrathoracic Surgery. Emil G. Beck, M.D., Chicago.

Studies in Intrapleural Tension. John W. Snyder, M.D., Rochester, Minn.

Remarks on the So-Called Mediastinal Septum of the Dog, in Relation to the Pneumothorax Problem in Man. Rudolph Matas, M.D., New Orleans.

A Reconsideration of the Question of the Effects of an Open Pneumothorax. Evarts A. Graham, M.D., St. Louis.

Graded Extrapleural Thoracoplasty in the Treatment of Diffuse Unilateral Bronchiectasis. Carl A. Hedblom, M.D., Rochester, Minn.

Bronchiectatic Pulmonary Abscess Simulating Apical Tuberculosis. Willy Meyer, M.D., New York.

Experimental Closure of Large Bronchi: A Study of the Factors Concerned in Failure of the Bronchi to Heal. Ralph Boerne Bettman, M.D., Chicago.

Abscess of Lung. Adrian V. S. Lambert, M.D., and James Alexander Miller, M.D., New York.

Proceedings.

List of Members of the American Associaiton for Thoracic Surgery.

COPYRIGHT, 1924, BY THE AMERICAN MEDICAL ASSOCIATION

ARCHIVES OF SURGERY

VOL. 8 MARCH, 1924 No. 2

PAGET'S DISEASE OF THE FEMALE NIPPLE

A PREVENTABLE DISEASE, CURABLE IN ITS EARLY STAGES: A STUDY OF THIRTY CASES

JOSEPH COLT BLOODGOOD, M.D.

BALTIMORE

The evidence for the conclusion that Paget's disease of the nipple may be a *preventable disease* is based on the observation of seven cases in which the lesion of the nipple healed under simple and protective treatment; in two cases there was a red, finely granular nipple, as illustrated in Figure 9, and there were five cases of warts, as illustrated in Figure 5. A sixth case, of a wart of long duration which disappeared under treatment, is described in Case 18.

The conclusion that Paget's disease is *largely curable* is based on the results in twenty cases in which operation was performed. In seven of these, the microscopic section showed no evidence of malignancy; two cases were examples of the red, finely granular nipple as shown in Figures 1, 2 and 9; three cases presented benign warts, as illustrated in Figure 5, and two cases, superficial ulcers on an as yet undestroyed nipple, as shown in Figures 13 and 14. These seven cases, in which operation was performed and the lesion found to be microscopically benign, exhibited very few clinical differences, except in degree, from the seven cases in which there was recovery without operation.

As evidence that Paget's disease of the nipple, microscopically malignant, is largely curable by early complete operation, there are twelve cases. In three of these, the glands showed metastasis, and there was at least 25 per cent. chances of a cure. At the present writing, one patient is dead; the remaining two are well, but have not yet completed the five-year period.

In nine cases, there was no metastasis to the axilla, and these patients had at the time of the operation at least 70 per cent. chances of a cure. At the present time, four patients have passed the five-year limit without recurrence, and one patient is dead of internal metastasis; the percentage of cure being 85.

The danger of incomplete operation is illustrated by one case in which the nipple only was removed; later, cancer developed in the breast, and the patient died of metastasis after the complete operation.

That Paget's cancer of the nipple as described by him, in which at the time of observation there is a palpable mass in the breast in addi-

tion to an ulcer of the nipple, is a hopeless disease is confirmed by our three examples, in which all the patients died of recurrence after the complete operation.

There is every reason to believe that the fourteen cases of lesions of the nipple were observed before malignant change and the thirteen cases of cancer of the nipple came to operation before a mass could be felt in the breast largely because of educational efforts. These women came under treatment earlier because they, or their physicians, had received correct information.

Paget as a Prophet.—Paget, in his original description, divined from his clinical and pathologic studies what he himself had not observed. In the first place, it was his opinion that the primary lesion of the nipple in which later cancer develops might heal spontaneously, especially when early appropriate treatment was given. I report here seven such cases. Again, he wrote that if it were his good fortune to see such a lesion of the nipple in the early stage before there was a palpable mass in the axilla, he would advise operation. I am now able to report twenty such cases in which the lesion was confined to the nipple only. Seven of these proved to be benign and thirteen cancerous.

BENIGN LESIONS OF THE NIPPLE WHICH HEALED WITHOUT OPERATION

The seven cases of benign lesion in which there was recovery without operation can be briefly described, because they do not differ from the next group in which the patients were subjected to operation. Two cases were examples of the red, finely granular nipple as illustrated in Figure 9. One was seen within a few days after the onset, the other within two weeks. No etiologic factor could be discovered. The Wassermann reaction was negative. One woman was married and had never nursed a child; in the other, it was years since the last lactation. Both first noticed that the nipple was red and itching; then the nipple began to exude a blood-stained secretion. The nipple was very red and finely granular, and the hemorrhagic secretion with the red nipple closely resembled a bleeding, edematous gum. The treatment consisted of washing with soap and water, and then with alcohol; then covering with silver foil. The dressing was done by the office nurse, and I watched the nipple almost every day until the condition was restored to normal, about two weeks. There has been no recurrence.

In the remaining five cases, the lesions were distinct warts, all unilateral, the size of, or larger than, the wart shown in Figure 5. In a few cases, the patients consulted us because of the wart; in others, the wart was found accidentally in a routine examination of the breast. The duration of the wart varied from months to years. The warts had never given discomfort; nor was there any evidence of scab for-

mation, or a history of bleeding or of the scab falling off. In these cases, the treatment consisted in daily washing with soap and hot water, followed by alcohol, after which the nipple was covered with white petrolatum. The patients continued the treatment until the wart disappeared. The time of complete healing varied from a few weeks to two or three months.

ETICLOGIC FACTORS IN CANCER OF THE NIPPLE

The study of the following twenty-three cases impresses me with the fact that cancer of the epidermis of the nipple begins as any other cancer of the skin or mucous membrane, irrespective of the etiologic factor. There is first a lesion of the mucous membrane or epidermis of the character of a wart, or an area of chronic inflammation. This often heals spontaneously without treatment; but if left alone and not protected, the ordinary trauma that the normal skin or mucous membrane frequently receives prevents healing; the affected area is more difficult to clean than the normal skin or mucous membrane; and there develops a definite wart or ulcer. The next change is the development of cancer, and after this, infiltration beyond the local area. Then follows involvement of glands, and internal metastasis.

All of the cases of lesions of the nipple demonstrated microscopically to be cancer exhibited ulcers, some with partial, others with total destruction of the nipple. In all of these, the clinical histories clearly picture two common types of onset. First, there is either a redness of the nipple, which soon becomes finely granular with different types of discharge, not always hemorrhagic; or there is a wart, or, in a few instances, a fissured or cracked nipple. The next stage is crust formation, which means superficial ulcer. From this point, cancer may be present or absent for varying periods. In one instance, it was absent for a period of two years; in two other cases, it appeared within eight months. The evidence would suggest that ultimately cancer develops in every ulcer of the nipple. The moment cancer develops in the ulcer of the nipple, there may be infiltration of the cancer cells along the ducts. As the ducts open directly through the epidermis of the nipple and as the epidermis of the nipple dips down into the duct, it is just as possible for the cancer to begin in the duct as in the ulcer. Of my thirteen cases of early cancer of the nipple, in only two were the ducts free from any evidence of cancer. The breast outside the ducts is less frequently involved in the early stage. In only four of the thirteen cases was I able to demonstrate nests of cancer in the lymphatics of the breast.

The axillary glands were involved in three of the thirteen cases. In one of these, there was no other evidence of cancer, except in the ulcer on the nipple; in a second, the cancer was present in the nipple and ducts; in a third, in the nipple, ducts and breast.

This is evidence of the danger of any unhealed lesion of the nipple and also clearly demonstrates that there is but one operation for cancer of the nipple, no matter how early, and that is complete operation.

Apparently, there is no relation between this type of lesion of the nipple and nursing. Twice it has occurred, or had its onset, in the cracked nipple of lactation. In all the thirty cases, the nipple has been retracted only once. The age of the patients with cancer of the nipple has varied from 38 to 84. The larger number of patients were past the menopause. So far, none have been in colored women.

Up to the present time, I have observed no syphilitic lesions of the nipple in women. There has been one syphilitic chancre in a male negro. This will be discussed in a second article on Paget's disease of the nipple in the male. Up to the present time, we have but two cases—one benign and the other a primary syphilitic sore.

Handley reports and illustrates in his recent book a typical example of Paget's cancer of the nipple in a male.

In discussing the cases in which operation was performed, I again and again consider the question as to when and how long one should attempt to treat an early lesion of the nipple by nonoperative means; when it is justifiable to excise a little lesion, such as a wart, as shown in Figure 5, and when one should consider excision of the nipple only for frozen-section study before resorting to the complete operation for cancer.

My whole evidence is against excision of only the breast. It is unnecessary when the lesion is benign, and not sufficient when the lesion is malignant.

When Paget's disease is seen in its latest stage, it is apparently hopeless from the standpoint of any treatment.

The evidence obtained from these histories would suggest that treatment with roentgen rays, radium or violet rays has little to offer.

BENIGN LESIONS OF THE NIPPLE SUBJECTED TO OPERATION (FIFTEEN CASES)

We may summarize thus the benign lesions subjected to operation:

1. Benign subepidermal nodule (adenoma) of the nipple (nine cases). In all of these, the nodule was of small size and, microscopically, resembled the varying types of encapsulated adenoma of the breast. In one of these, the surface of the nipple over the nodule had a red, finely granular appearance with superficial ulceration—the only one which suggested the beginning of Paget's disease.

2. Warts (three cases). One was the seat of a minute superficial ulcer and suggested the beginning of Paget's disease.

3. The typical red, finely granular nipple without a subepidermal adenoma, suggesting the beginning of Paget's disease (one case).

4. Superficial ulcer of the nipple; in which the nipple was partly or completely destroyed, microscopically not cancer, yet clinically identical in appearance with the cases in which the sections clearly pictured Paget's disease in the malignant stage (two cases).

Of these fifteen cases, seven had the clinical picture of a wart with or without ulcer, one, the typical red, finely granular nipple without ulceration, the other, slight beginning ulceration; the remaining two cases had gone on to the definite stage of ulceration with scab formation, and in one the nipple had been practically destroyed. In only one of these was a subepidermal adenoma found; and, as there have been

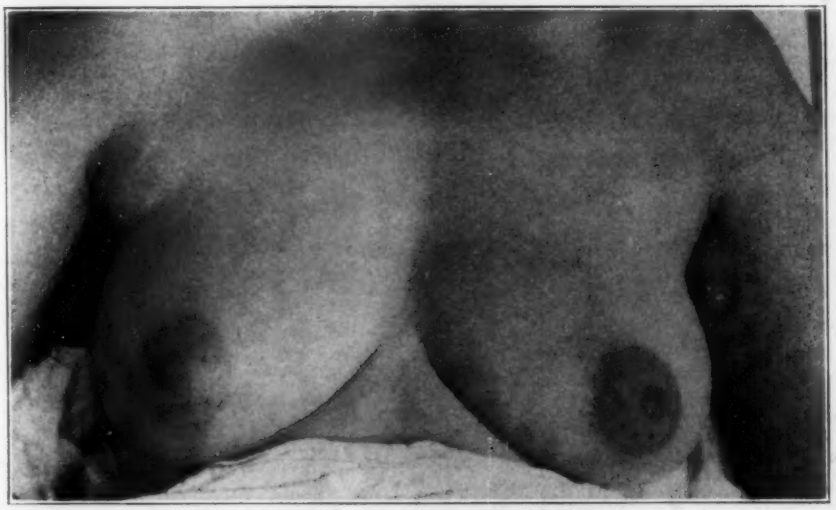

Fig. 1 (Case 1).—Example of the finely granular, red nipple. The little granules on the top of the right nipple are better pictured in Figure 2.

eight examples of subepidermal adenoma without a wart, the finely granular red nipple or the ulceration, we can easily conclude that there is no relation between a subepidermal adenoma and Paget's disease of the nipple. As we will show in the later cases (sixteen) of the malignant stage of Paget's disease, no remains of a preëxisting subepidermal adenoma could be demonstrated. I am emphasizing this here because the evidence of the seven cases which healed without operation and of the seven cases subjected to operation indicates that Paget's disease begins either in the epidermis of the nipple, or in the downgrowth of epidermis into the opening of the ducts, and therefore its etiologic factor and origin are not unlike that of any benign or malignant epithelial growth arising in the skin.

REPORT OF CASES

CASE 1.—*History.—Benign subepidermal nodule over which the skin of the nipple has the finely granular, red appearance.* (Figs. 1, 2, 3 and 4.) The patient, a white woman, aged 44, married, observed in December, 1919, with no history of pregnancies, was unable to give any etiologic factor. Eighteen months previously, she observed an area on top of the nipple which was distinctly red and finely granular, and during the intervening months other minute red granules appeared. There had been no itching, but a stinging sensation for one year. The patient had observed no weeping and no discharge of any kind. The

Fig. 2 (Case 1).—Finely granular, red nipple in specimen. The roughness of the top of the nipple, which, in the fresh specimen, was very red, may be observed (see Figure 1).

condition had been diagnosed eczema and treated with ointment, but only intermittently.

Examination.—The top of the right nipple was rough and granular, as shown in Figure 1. The little elevations were red, and here and there were white nodules. Beneath the right nipple, I could palpate a minute pea-sized nodule. Nothing could be made out in either breast, on palpation.

Operation.—In December, complete excision of right breast was performed. At that time, it was my opinion that this was the early stage of Paget's disease and that excision of the breast was sufficient.

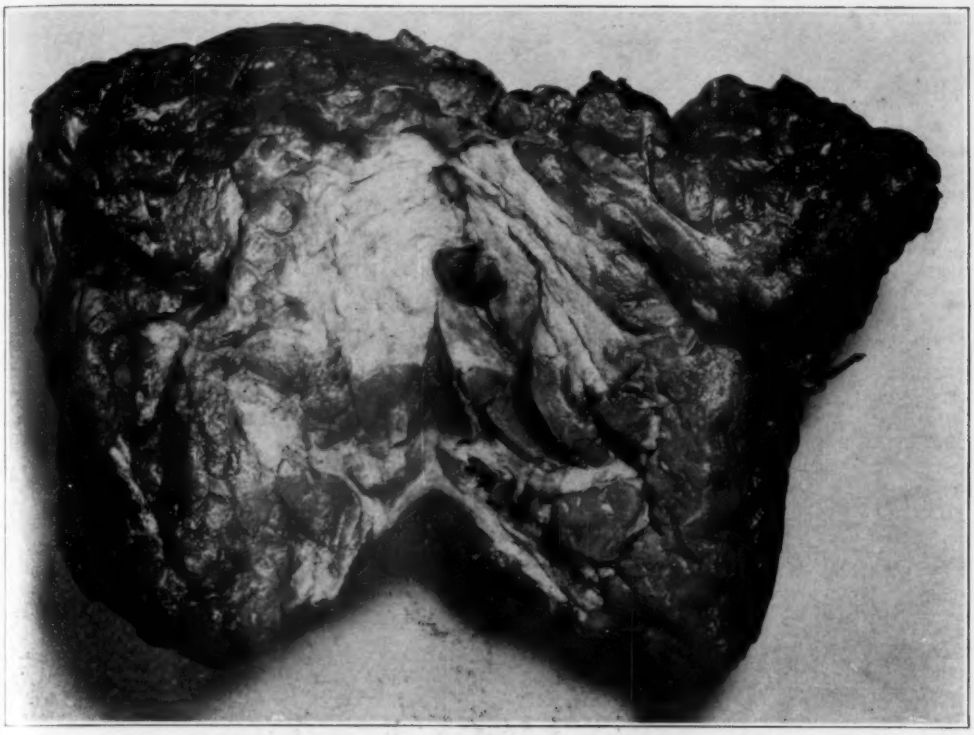

Fig. 3 (Case 1).—Section through the breast shown in Figure 2. The encapsulated brown tumor is an adenoma (see Figure 4). It is surrounded by white breast tissue. The little nodule above is the base of the nipple. The tissue on the periphery is fat mixed with white breast tissue.

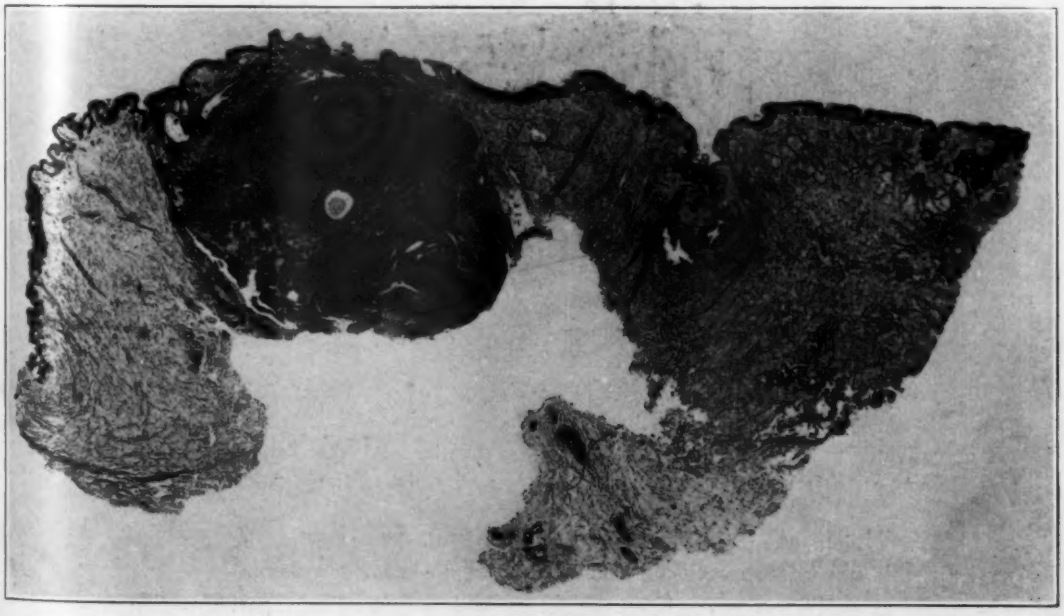

Fig. 4 (Case 1).—The entire section through the nipple and subepidermal adenoma shown in Figure 2. The epidermis of the nipple, especially over the nodule, shows slightly hypertrophy and little nodules of overgrowth. There is no ulceration.

Pathologic Examination.—Gross pathology: Figure 2, a photograph of the excised breast, shows better than Figure 1 the rough, finely nodular surface on top of the nipple. We could discern no definite ulceration. Figure 3, a gross section through the breast, shows at *X* the encapsulated adenoma surrounded by white, normal breast tissue and then the surrounding fat.

Microscopic pathology: Figure 4 pictures in a low power the encapsulated adenoma and the surface appearance of the nipple, which lies above and to the left of this nodule. In the epidermis, there is nothing particularly abnormal, except the numerous little nodular projections of the epidermis. With the high

Fig. 5 (Case 2).—Benign wart on nipple with a minute ulcer. For microscopic sections, see Figures 6 and 7.

power, I could see nothing in the epidermis to suggest Paget's disease. There is some hypertrophy, with here and there minute elevations. There is no explanation for the redness observed clinically, and the little nodules are apparently irregular overgrowths of the epidermis of the nipple. Numerous sections of the breast show no abnormality.

The histologic pictures of the subepidermal adenoma will not be reproduced as this tumor is an accidental finding and of no importance here.

Outcome.—Two years later, the patient and her physician report that she is well. Since then, she has changed her address without notifying me.

If I examined this patient today, I should not operate at once, as there were no signs of ulceration, no weeping and no induration of the nipple. I should employ twice daily washings with hot water and soap and protect the nipple with silver foil or petrolatum. If the lesion did not heal in ten days, I should excise the nipple and the nodule under procain, and if the frozen section resembled what we found, I would

Fig. 6 (Case 2).—Section, under low power, of wart shown in Figure 5; hypertrophied epidermis to the right and granulation tissue to the left, with irregular nests of epithelium on the surface of the ulcer (see Figure 7).

not remove the breast. The patient was a young woman and she would be saved this unnecessary deformity. Following are three cases of benign warts of the nipple:

Case 2 (Figs. 5. 6 and 7).—This observation is of great interest because the small wart was the seat of a minute ulcer, and in this ulcer we find the micro-

scopic picture of what appears to be Paget's disease in its earlier stage. In this case, only the wart with a margin was excised in 1919, and in 1923, four years later, there is no evidence of recurrence.

Figure 5 shows the wart on the nipple, but not the minute ulcer. The patient, a white woman aged 38, had observed the wart for six months; about two months previously, there was itching, and two weeks previously, slight weeping. It was twelve years since she nursed her last child, and there was no history of trauma. The wart was visible and palpable. The minute ulcer from

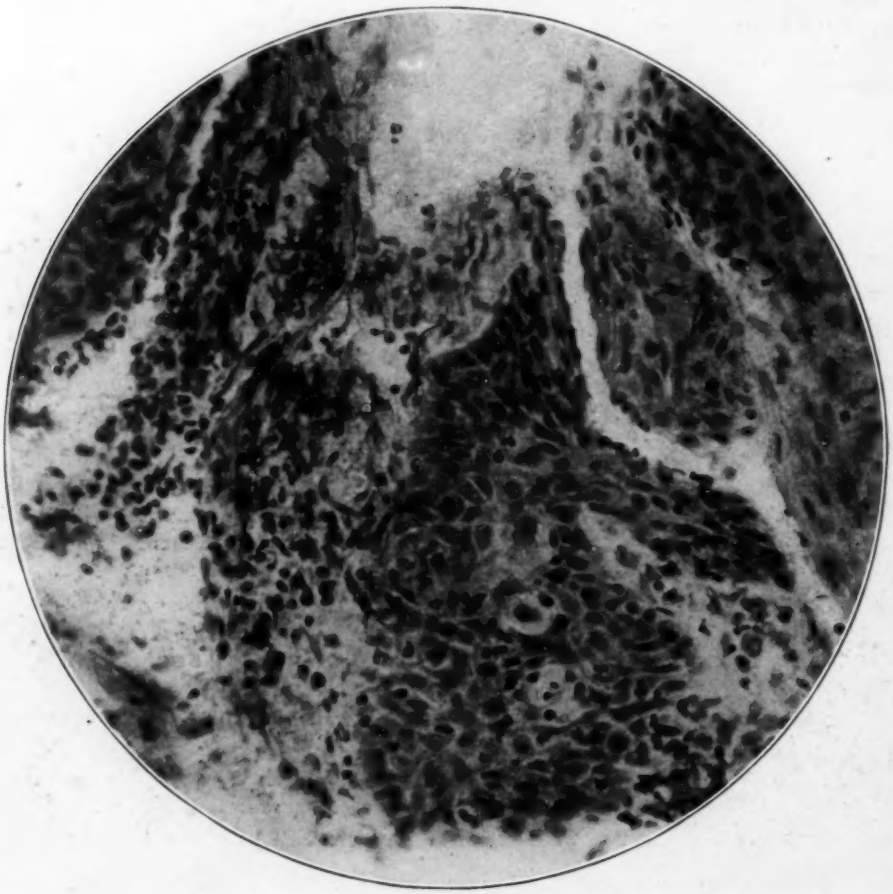

Fig. 7 (Case 2).—Section, under high power, shows irregular masses of epithelium in the granulation tissue of the ulcer shown in Figure 6. Among these epithelial cells are many of the typical Paget cells (compare with Figures 14, 19 and 20).

which the slight discharge came can be seen. There was no induration of the nipple about it. The other nipple was normal and no nodules could be palpated in either breast.

Figure 6 shows, with the low power, the epidermis of the wart to the right and the ulcer with atypical growth of epithelium to the left. Figure 7 is an

area of epithelium in the ulcerated area (high power). Microscopically, it has the appearance of a benign epithelial growth in granulation tissue, but morphologically the cells, especially the vacuolated cells, are apparently identical with those of the fully developed stage of Paget's disease.

As I will again emphasize, this epithelial overgrowth of the nipple, whether benign or malignant, contains cells of a morphology different from that of the ordinary wart or cancer of the epidermis. The Paget lesion is neither a basal-cell nor a spinal-cell tumor, but somewhat resembles the transitional-cell epithelioma of the bladder.

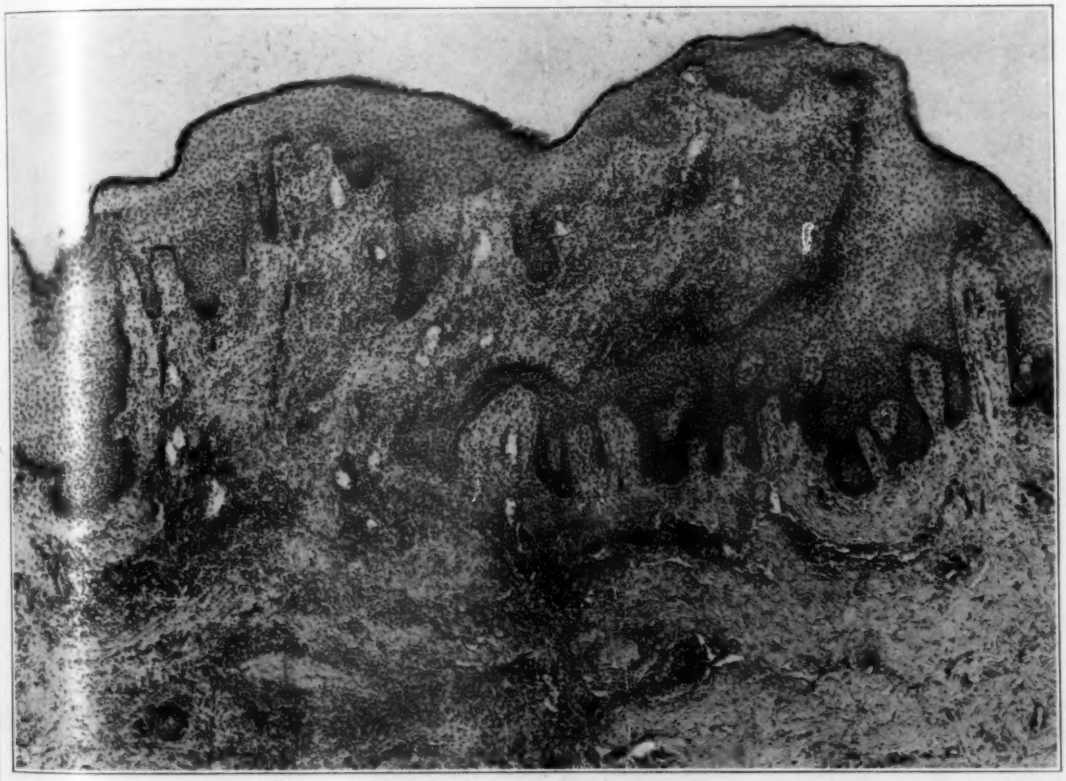

Fig. 8 (Case 4).—Section, low power, of benign wart on nipple. The high power shows cells of the Paget type (see Figure 7).

CASE 3.—This wart was more of the form of a papilloma, and the sections show the benign epithelial growth with cells *not* of the Paget type. It was removed by Dr. Brown of Winchester, Mass., in 1915, apparently with the nipple. The patient was 43 years of age. The duration of the lesion was not given.

I advised against further operation, and there has been no recurrence.

CASE 4 (Fig. 8).—Dr. R. B. Morris of Olean, N. Y., excised this little wart from the nipple in 1913. He describes it as a small, reddish growth on the skin of the nipple.

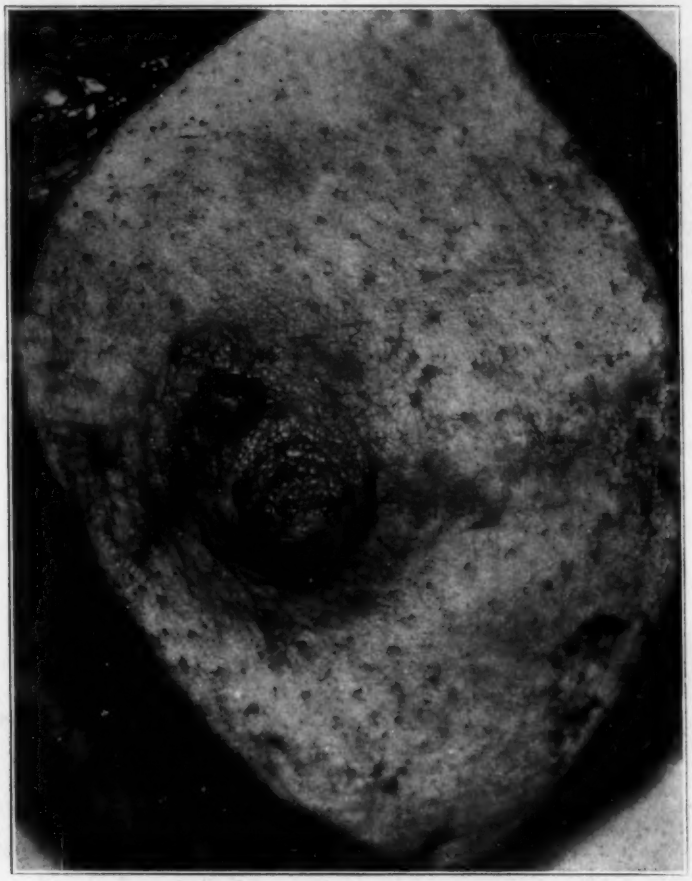

Fig. 9 (Case 5).—The breast after removal. The typical, fully developed, finely granular, red nipple in the benign stage, much more evident than in Figures 1 and 2. The upper portion of the nipple and areola are involved. The nodule to the left and above is a supernumerary nipple. For microscopic appearance, see Figures 10 and 11.

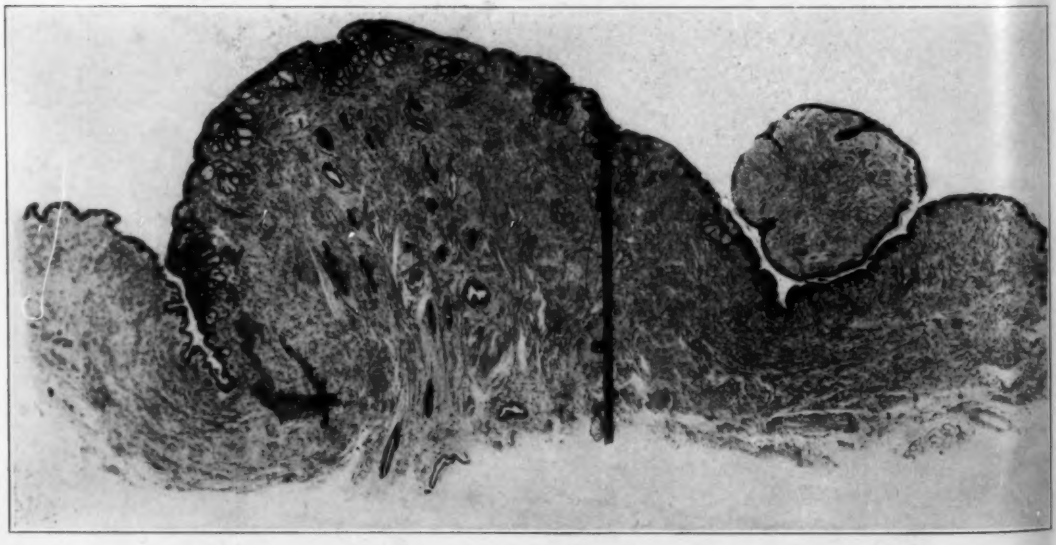

Fig. 10 (Case 5).—The entire section through the nipple and supernumerary nipple shown in Figure 9. There is no marked evidence of disease. For higher power, see Figure 11.

Figure 8 pictures a benign warty growth with a subepidermal inflammatory reaction and increased vascularity, but there is nothing in the morphology of the cell, as compared with those shown in Figure 7, to suggest that it resembles typical Paget's disease.

About one year later, Dr. Morris removed the breast, because it was painful. There was no gross evidence of malignancy. Two years later, he reported that the patient was well.

CASE 5 (Figs. 9, 10 and 11).—*The benign stage of the red finely granular nipple.* Figure 9 shows the excised breast. The little nodule above and to the

Fig. 11 (Case 5).—Low power of a portion of the surface of the finely granular red nipple shown in Figures 9 and 10. Between the arrows, above, is an area of hypertrophied epidermis containing cells of the Paget type (see Figure 7).

left is a supernumerary nipple. The upper one-half of the nipple and areola has a finely granular surface which in the living specimen was intensely red. The lower half has the normal appearance.

Figure 10 shows the entire nipple and the supernumerary nipple under low power; sections of the ducts are seen in the nipple. The surface of the epidermis is a little rougher than normal and in places the epidermis is thicker.

With the high power (Fig. 11), we observe that the epidermis is thicker and in one area (indicated by arrows) the thickened epidermis shows splits and a definite change in the morphology of the cells. With the high power, these cells resemble those in Figure 7 and are seen to be of the Paget type.

I examined this patient in February, 1921, but at that time I had not yet started on this investigation of Paget's disease. She was an unmarried woman, aged forty, a sister in the hospital. She had observed the fine, red granules four weeks, and there has been definite weeping of a slightly purulent secretion. On palpation, there was no induration of the nipple. It resembled closely the lesion

Fig. 12 (Case 6).—Section, low power, of edge of a benign ulcer of nipple. The area of hypertrophied epidermis between the arrows is identical with the area in Figure 11, and both contain cells of the Paget type as shown in Figure 7.

shown in Figure 1, but, as can be seen, it was much more distinct, although of but four weeks' duration; while the lesion in Figure 1 was of eighteen months' duration. I looked on it as the early stage of Paget's disease, and removed the breast.

Serial sections through the nipple and the breast showed no malignant change. In the breast tissue, there was very little parenchyma—chiefly fat and fibrous tissue.

This patient is well (1923) after two and one-half years.

Now that I have thoroughly studied my cases of Paget's disease, I should give a case of this kind the preliminary treatment—hot water and soap, silver foil or petrolatum. In view of the results in two somewhat similar cases previously mentioned here, the chances are that the lesion would have healed. If not, I would excise the nipple under procain and study the frozen sections, acting on the findings. At that time, although I did not think that the condition was cancer, I felt that it was safer to excise the breast.

Following are two cases of benign ulcer of the nipple:

CASE 6.—Dr. Churchman, then resident surgeon of Johns Hopkins Hospital, excised the nipple from this patient in 1909, and after studying the sections with Dr. Bird in the laboratory, decided that there was no evidence of malignancy.

Figure 12 shows the hypertrophy of the epidermis near the ulcer. At *X*, between the arrows, the entire thickness of the hypertrophied epidermis shows the changed morphology of the cells of the typical Paget type pictured in Figure 7 and the characteristic splits and crevices shown in Figure 11.

The patient, a white woman, aged 49, did not give the usual history of a wart, or the red, finely granular nipple, but of a cracked nipple, a condition with which she was familiar, because she had nursed eleven children, the last some years ago. The crack or fissure was of ten months' duration. There were a purulent discharge and a scab; pain and soreness, and intense itching. The crack increased in size, and there was a definite ulcer. A similar area appeared on the left nipple, but healed. The area of the right nipple increased in size. It was the itching and burning that brought the patient to the clinic.

On examination, it was seen that the affected nipple was not completely destroyed. The remaining portion of the nipple was enlarged and red. The ulcerated area was covered with a crust; the skin of the nipple and areola was thickened and indurated. There was no marked tenderness. The left nipple showed no evidence of the lesion which the patient described as having healed. There were no nodules in either breast.

Six years later, in 1915, the patient wrote that there had been no further trouble in the right breast, but had been a recurrence in the left nipple, which had again healed.

The clinical picture in this case, illustrated in Figure 12, and the appearance at examination are typical of the disease as described by Paget, as far as the involvement of the nipple goes. It resembles closely the ten cases which I will soon describe, in which the microscope revealed that the nipple region was cancer, and in two of these cases the duration of the lesion was only eight months.

Therefore, in a case of this kind, unless one is prepared to make the microscopic differential diagnosis between the benign and malignant stages of Paget's disease, it would be safer to perform the complete operation for cancer. The lesion of the nipple in this case had passed far beyond that pictured in Figures 1, 5 and 9. It is fair to say that it was good fortune rather than good diagnosis that led to the result in this case, because at this time none of us in the laboratory were

really familiar with the histologic appearance of Paget's disease of the nipple. This is proved, because in a second case, in which the operator removed only the nipple and the pathologist diagnosed the lesion benign, there was a rapid recurrence and death from cancer.

CASE 7 (Figs. 13 and 14).—This case is of unusual interest, because it is our only example of Paget's disease occurring in a congenitally contracted nipple.

Figure 13 is a gross section through the nipple and the breast beneath. The breast tissue is largely fat. There is a little stroma beneath the nipple. The remains of the nipple are shown at *X*; the inversion has disappeared in the gross specimen. The nipple was largely destroyed by an ulcer.

The microscopic appearance of this ulcerated, retracted nipple is shown in Figure 14. Here, we have the typical morphology and splitting characteristic of Paget's disease of the nipple in a much more advanced stage than that pictured in Figures 7 and 11. On the surface, there is a zone of hornified epithelium; then, there is a deeper zone of the Paget cells. As can be seen, there is no infiltration at the base, and although I have classified the condition as the

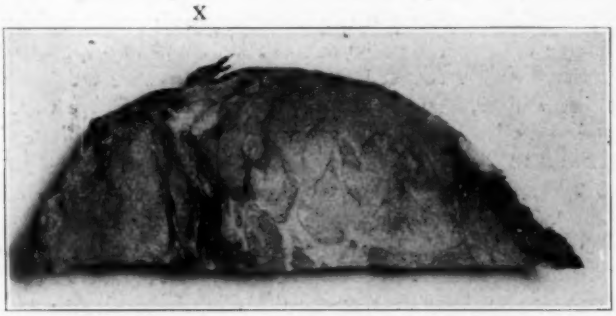

Fig. 13 (Case 7).—Gross section through the remains of the nipple and the senile fatty breast. The nipple (*X*) is surrounded by an ulcer. For microscopic section, see Figure 14.

benign stage of Paget's disease, if I excised a nipple the seat of a lesion suspicious of Paget's disease, I would perform the complete operation for cancer.

Further microscopic studies of this breast and of the axillary glands showed no evidence of malignancy or metastasis.

The history and examination of this patient suggested to me Paget's disease in the malignant stage, but it was no more clearly malignant than the one just described in the previous case.

The patient, a white woman, aged 49, married, but with no children, stated that the left nipple had always been contracted, and she thought that four years before operation there was a little brownish discharge through the slit in the retracted nipple. A free interval of about two years followed. Then the discharged recurred, with tenderness. At this time, two years previously, radium treatment was given, being continued until a few months ago. The discharge ceased and crusts filled the slits. The slits enlarged, and the skin of the areola about it became dark red. For the past three months, there had been more pain and now and then a little weeping. In addition to radium treatment, the violet rays had been used and different kinds of ointment applied.

On examination there was no lump in either breast. The right nipple was normal. The retracted left nipple could be seen through the slit, which was covered with a scab. On palpation, it was distinctly indurated. The definite ulceration and partial destruction of the nipple were not observed until the specimen was examined. The redness of the areola described by the patient was not present.

In view of this history and examination, I performed the complete operation, in 1919, and the patient is well four years later.

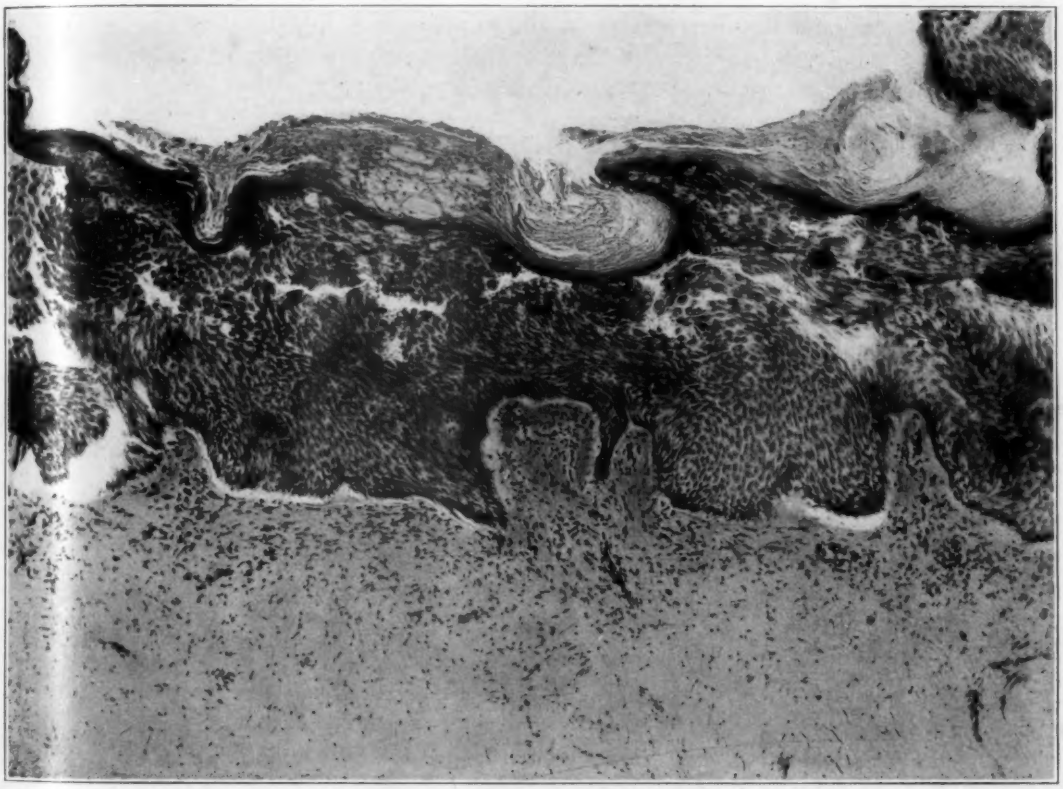

Fig. 14 (Case 7).—Section through the ulcer surrounding the partly destroyed nipple shown in Figure 13. In this epithelial overgrowth, there are cells of the distinct Paget type (Fig. 7). The appearance is more malignant than in Figures 8 and 12.

In this case, the breast showed no dilated ducts, nor minute papillomatous cysts to explain the brownish discharge four years previously. The probabilities are there was an ulcer then, which healed. But for two years the symptoms had been continuous, and the patient ran great risk of the formation of a fully developed cancer during the treatment which is not based on carefully studied evidence.

I trust all who read this paper will study Figure 14, as it will indicate to them the difficulties they may meet in excising a nipple and then deciding from the frozen section whether to perform the complete operation for cancer or not.

Although I have classified this case with the benign group of Paget's disease, I wish to emphasize again that, with our present knowledge, it would be safer to look on a frozen section similar to Figure 14 as an indication for the complete operation for cancer in a lesion of the nipple. In the previous cases, except Case 6, the clinical picture as well as the frozen section would amply justify excision of the nipple only.

The Early Stage of Paget's Cancer of the Nipple.—A distinct ulcer is present, but the nipple is not yet destroyed. In all of these ten cases, the disease was observed and operation was performed before there was any lump in the breast to be palpated; that is, it was a stage of Paget's disease which he described as antedating the stage in which it was his ill fortune first to observe it. The most remarkable part of Paget's description is that pertaining to the condition of the nipple which antedated the cancer of the breast.

In all of these cases, the microscopic appearance of the lesion on the nipple in the ulcer is practically identical. In two, no minute areas of cancer were found in the ducts beneath the nipple, nor in the breast. Yet, in one of these, the axillary glands showed metastases. In four, small nests of cancer were found in the ducts beneath the nipple. In none of these four cases did the axillary glands show metastases, nor was there any evidence of cancer nests in the breast.

In the remaining four cases, in addition to the cancer of the nipple, and cancer nests in the ducts, there were microscopic areas of cancer in the breast. In only one of these did the glands show metastases.

It is important to remember that all these cases have been restudied with new sections, and the only conclusion that I can come to is that the primary carcinoma originated in the epidermis of the nipple, and had its origin in benign lesions, seven of which I have previously described. The involvement of the ducts and the breast is secondary. That of the ducts appears to be a definite downgrowth, just as we would expect, because the point of least resistance for the growth of these cells would be along the ducts. The involvement of the breast is apparently through the lymphatics, just as the involvement of the lymphatic glands.

These cases demonstrate that a relatively small ulcer not yet destroying the nipple may be cancer, and it is impossible to tell by palpation whether the ducts, breast or axillary glands have become involved. Therefore, there can be but one rational treatment for a

lesion of this kind—the complete operation. An ulcer of the nipple may be just as distinctly cancer and just as dangerous as a cancer lump in the breast. It is important to remember that Paget never saw the disease he described, in its early stage. The duration of the known lesion of the nipple in these ten cases has varied from eight months to three years. Cancer, therefore, may develop in the benign lesion of the nipple within eight months and may still be confined to the breast after three years, because in one of the cases of three years' duration the axillary glands were not involved. The duration of the disease in the two cases in which the axillary glands showed metastasis was one year. The duration of the known nipple lesion in the seven cases here described as benign was relatively short. The warts were of from two weeks' to six months' duration; the red granulation of the nipples of from four weeks' to eighteen months' duration; and the two cases typical of Paget's disease with ulcer and scab of ten months' and two years' duration. But it must be remembered that we are very suspicious of the microscopic appearance shown in Figure 14, the one we called benign ulcer of two years' duration.

It would be safer to look on a definite ulcer of the nipple of more than three months' duration as clinically very suggestive of cancer.

Following is a case of cancer of the nipple with no involvement of ducts, breast or glands:

CASE 8.—The frozen section at the operation in this case was diagnosed cancer by Dr. Straight of Bradford, Pa., formerly a student in my laboratory. Thereafter, the complete operation for cancer was performed by Dr. Benninghoff, in 1916. This section is still in the laboratory, and the patient is well today, seven years later. Dr. Straight sent me the following history:

The patient, a white woman, 38 years of age, had a small scab no larger than the head of a pin for one year. When this scab fell off, there was blood-tinged weeping. Three weeks previously, a larger scab came off, and there was more discharge of blood and pus. Now for the first time the patient consulted a physician, Dr. Martin of Salamanca, N. Y., who advised immediate attention by a surgeon. The ulcer was but 5 mm. in diameter; the surrounding skin looked red. There is no note on induration.

Here is a demonstration of how minute the ulcer may be and yet be malignant. This is true of the skin anywhere and of the mucous membrane of the mouth.

Had this patient consulted a physician at once, simple treatment of the minute scab might have accomplished healing within a few weeks. If this had failed, excision of the nipple and frozen sections might have demonstrated the lesion to be still in the benign state.

I was sent sections not only of the nipple, but also of the breast in this case, and I was unable to find any evidence of cancer beyond the nipple. Dr. Straight reported no metastasis to the glands. My studies of the breast and ducts were based on nine different sections.

Following is a case of cancer of the nipple, with no involvement of ducts or breast, but metastasis to the basal glands in the axilla:

Case 9 (Figs. 15, 16, 17 and 18).—Figure 15 is a section through the superficial ulcer on the involved nipple, and we can see the infiltration from the epidermal growth. It is histologically cancer. Sections of the basal axillary glands which showed carcinoma proved its malignancy. The morphology of the cells is identical with that in Figures 7 and 14.

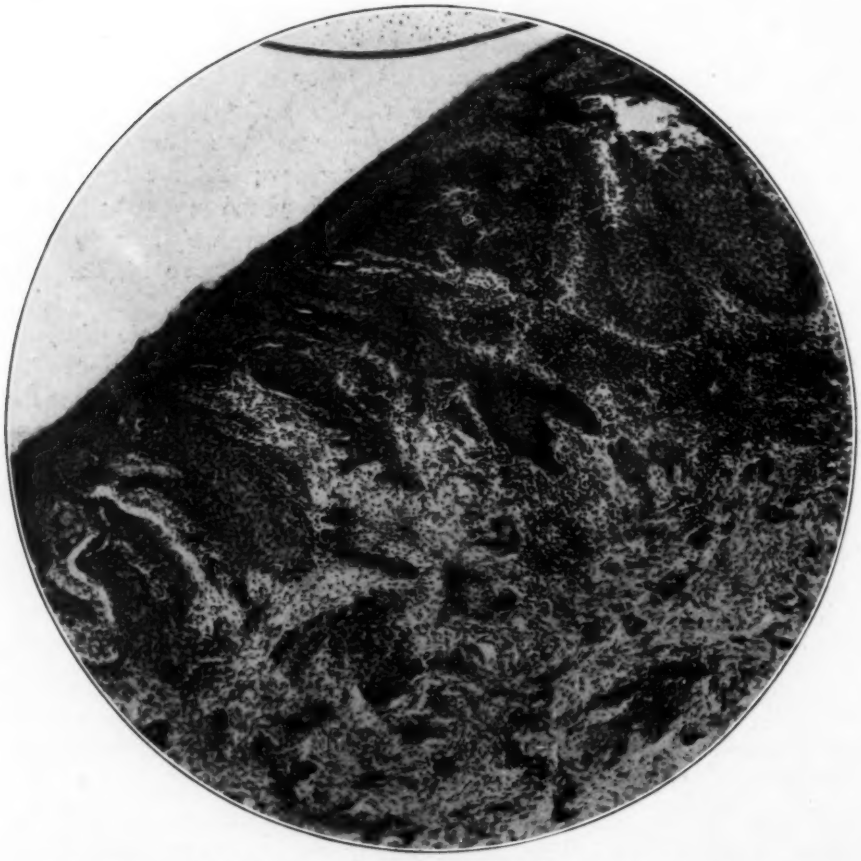

Fig. 15 (Case 9).—Cancer in superficial ulcer of the nipple, which is not completely destroyed (low power). With the high power, cells of the Paget type are seen.

Figure 16 is a section through an area near the ulcer and shows the hypertrophy of the epidermis, and the epithelial downgrowth at *X* shows the changed morphology of the cell. This should be compared with Figure 11.

The examination was negative, except as to the left nipple (Fig. 17). It was smaller than the right, but stood out prominently. The nipple was very red and over about one fourth of its surface as shown in the photograph there was a superficial ulcer. The nipple was indurated and felt like a fibroma. There was

no induration beneath the nipple, nor in any part of the breast. The glands in the axilla were just palpable. The lesion had been present for one year in a woman now 60 years of age, married, but with no children. In the beginning, the nipple was red, finely granular and sensitive, and there was a blood-stained discharge.

I felt it safer to perform the complete operation for cancer. This was done in February, 1923. At the present time the patient is well (July, 1923).

The section through the nipple and the breast (Fig. 18, below) shows that the diseased nipple was sharply outlined from the remaining senile and fibrous

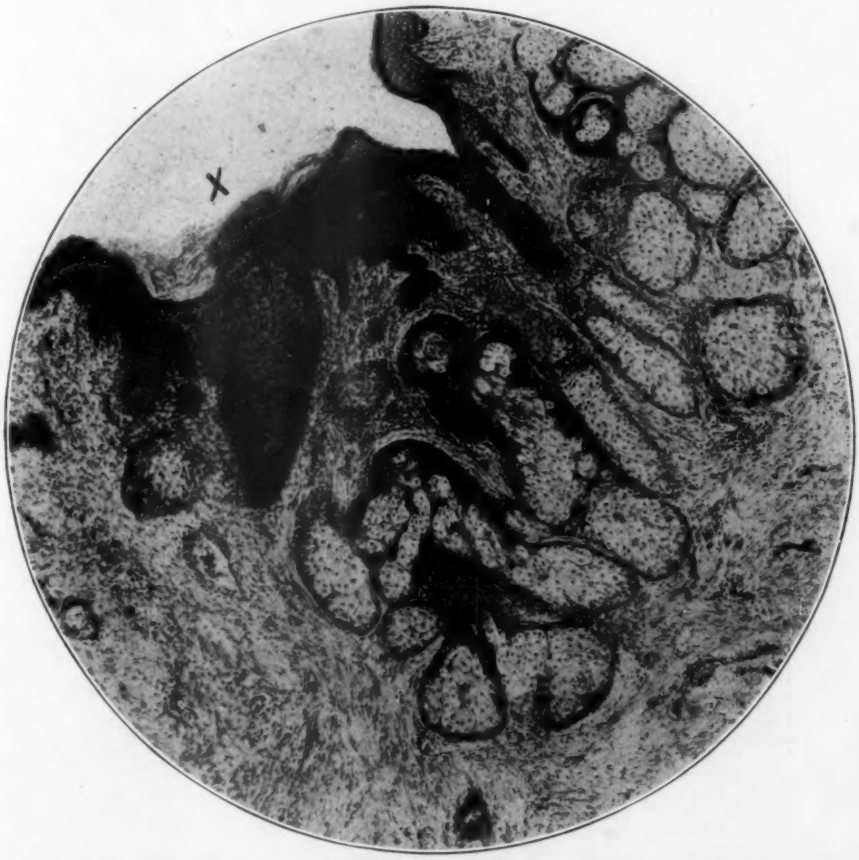

Fig. 16 (Case 9).—The epidermal edge of the cancer-ulcer shown in Figure 15. At *X*, there is an area of beginning hypertrophy of the epidermis and cells of the Paget type. For the gross section, see Figure 18.

breast beneath it. In Figure 18, above, the base of the nipple is sharply circumscribed from the surrounding breast tissue. Serial sections through the breast failed to reveal any nests of cancer cells. Sections of the mid and apex glands in the axilla were negative.

This case proves that a cancer of the nipple demands the same complete operation as a cancer of any other part of the breast.

Four cases of cancer of the nipple with microscopic cancer involving the ducts only, and no evidence of cancer of the breast and no metastasis to the glands are reported.

CASE 10 (Fig. 19).—The interesting point about this observation is that only the breast was excised, and the patient, now aged 78, is apparently well today

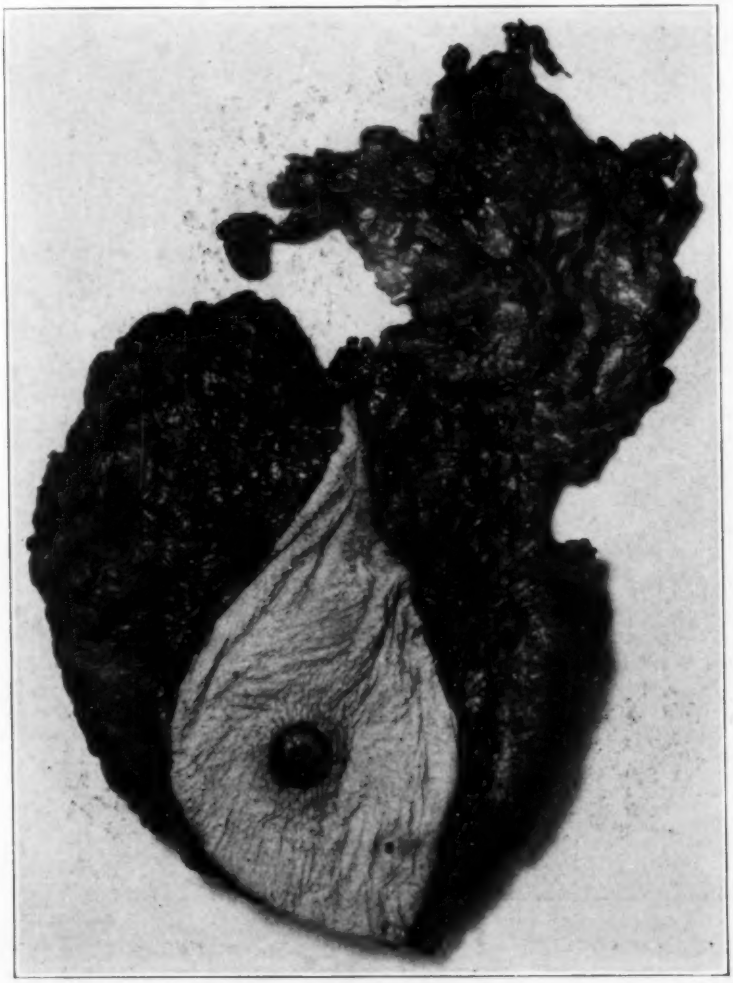

Fig. 17 (Case 9).—Specimen after complete operation. The nipple was prominent, red and indurated. The superficial ulcer is seen below to the left. There were no changes in the skin of the areola. For microscopic appearance, see Figures 15 and 16; for gross sections through nipple and breast, see Figure 18.

six years after operation. I am confident that I took a risk in removing the breast only, but the patient was very feeble and 72 years of age. The lesion on the nipple resembled that shown in Figure 17; a prominent, red nipple with

a smaller ulcer. It had been present eight months. Her attention was called to it by itching, and she observed the redness of the nipple. Weeping had not been a prominent sign.

When examined, the nipple was elevated and red, but not finely granular; the ulcer was covered with a scab; the epidermis of the areola was redder than normal, and the nipple was distinctly indurated. There was nothing to be palpated in the breast.

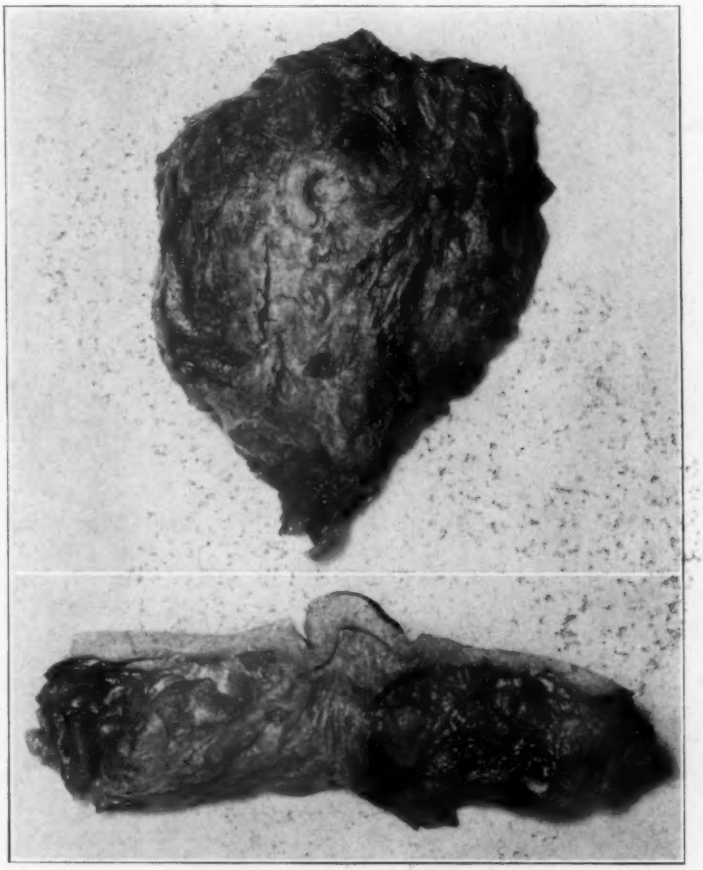

Fig. 18 (Case 9).—Below: Section through nipple and breast. The nipple is sharply outlined. The breast beneath in the gross and in the microscopic section shows no evidence of cancer. Above: The appearance of the base of the nipple and surrounding breast. For microscopic sections, see Figures 15 and 16.

The morphology of the cells was that of Paget's disease (Fig. 19). The infiltration was not so marked as in Figure 15. The section was not unlike the one shown in Figure 14, but as I found distinct evidence of cancer nests in the ducts beneath the involved nipple, I have placed this case in the cancer group.

CASE 11 (Figs. 20, 21 and 22).—A high-power photomicrograph (Fig. 20) from the ulcer of the nipple shows well the typical morphology of the Paget cells. To the right, we can see a few nests of cancer cells in the inflammatory reaction.

Figure 21 illustrates Paget cancer cells in a duct of the nipple below a portion of the epidermis of the nipple which is not yet involved or infiltrated by cancer.

Fig. 19 (Case 10).—Section, low power, of ulcer of the nipple. The narrow zone of epithelial cells and the subepidermal lymphoid zone. Although there is no evidence of cancer beneath this zone, cancer nests were found in the ducts. Compare with Figure 14, in which no cancer nests were found in the ducts.

With the high power, the cells in this duct resemble the cells shown in Figure 20. The appearance of the nipple in this case resembled that in Figure 17, but the

ulcer was larger, the nipple less prominent (Fig. 22). In Figure 22, above, dilated ducts both in the nipple and in the breast beneath it may be observed. Cancer was found in some, but not in all of them; there was no evidence of cancer outside the ducts, nor in the glands.

The diagnosis of Paget's cancer was made by Dr. William A. Fisher of Baltimore, and the complete operation was performed by him, in 1919. The patient is well, four years later.

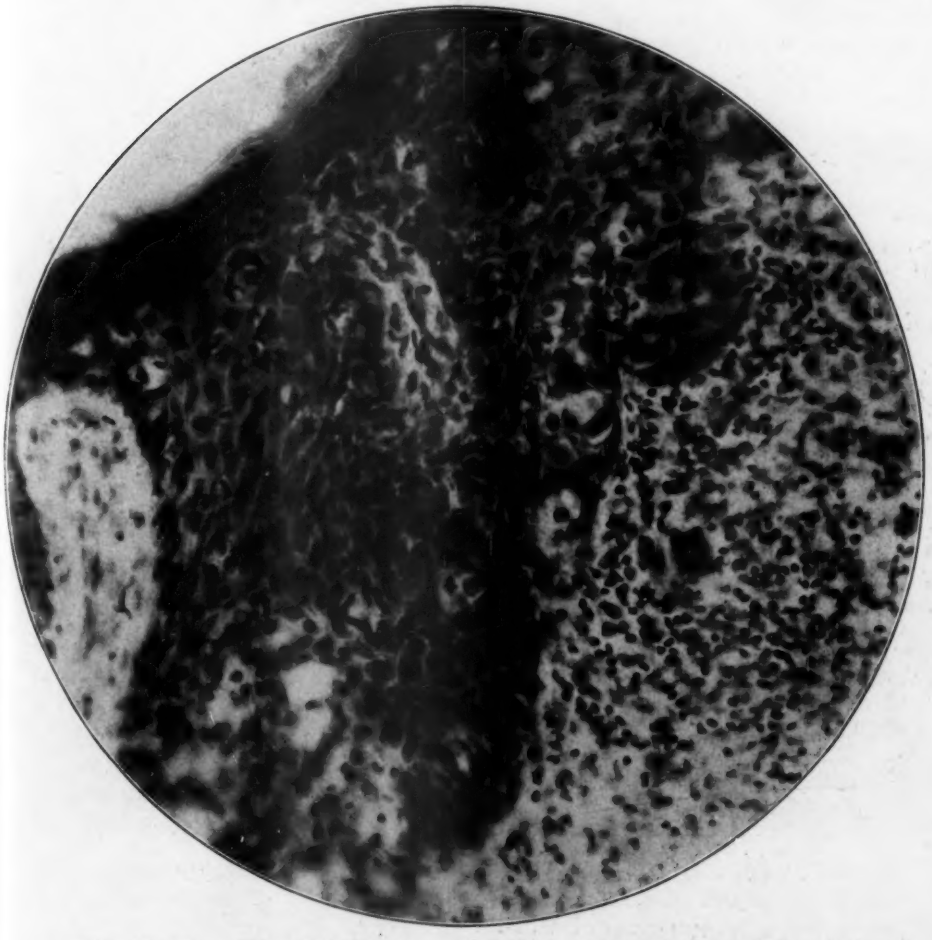

Fig. 20 (Case 11).—Microscopic section, high power, of ulcer of the nipple; typical Paget cells, evidently cancer. There are nests of cells in the granulation tissue below the epidermal tumor. Compare with Figures 7, 14 and 19.

Dr. Fisher gives the clinical history and describes the findings at examination as follows: The patient, aged 64, had nursed her children without difficulty. For eighteen months, she had had trouble with the nipple which was diagnosed eczema. At first, the nipple was red; then there was weeping of serum; then scab formations and crusts appeared. When the scab came off, the surface wept. There had been burning and itching. There had been no other areas of eczema

on the skin. The involved right nipple (Fig. 22) was slightly retracted and definitely indurated, but there were no indurations in the breast.

CASE 12 (Fig. 23).—This case represents the only postoperative death, from an embolism some days after operation, in a patient 84 years of age. I am still of the opinion that Dr. Wheeler was wise in performing the complete operation, as the danger of death from embolism was certainly less than the probability of involvement of the axillary glands. The appearance of the nipple (Fig. 23) closely resembled that in Figure 22, in that the nipple is slightly retracted. The minute dilatation of the ducts in the nipple is seen, and the ducts only were involved.

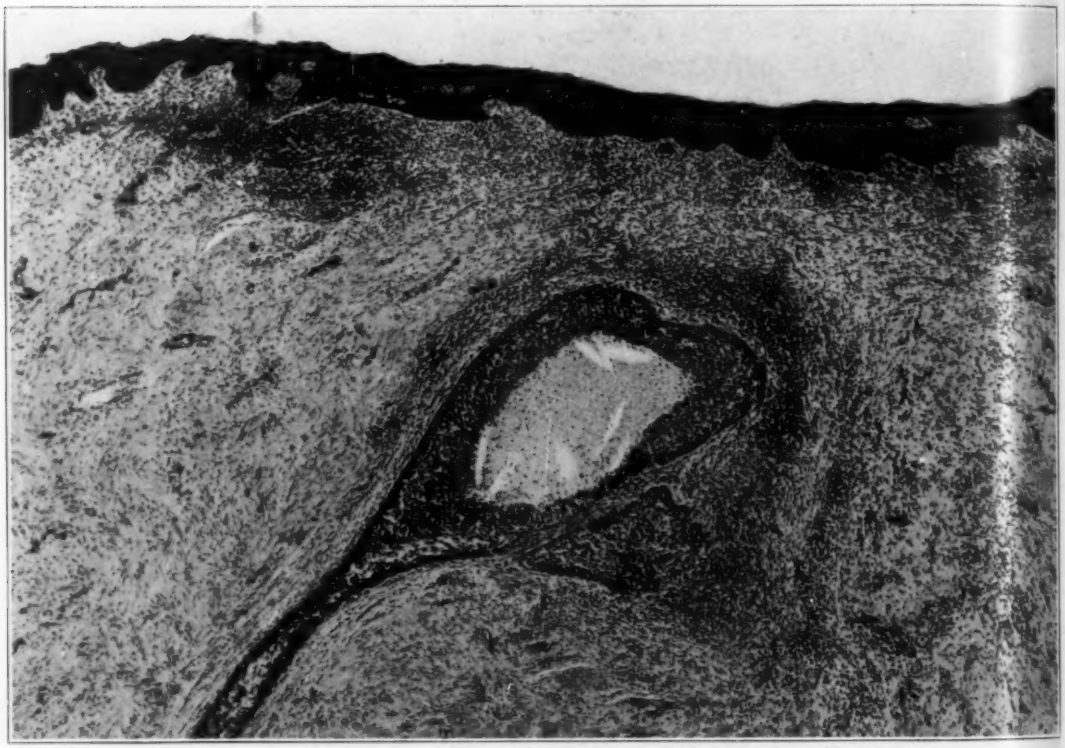

Fig. 21 (Case 11).—Cancer cells of the Paget type in a duct, beneath normal epidermis. See Figure 20 for the section of the cancer of the nipple in this case. For gross picture, see Figure 22.

Perhaps this patient could have been protected from cancer if immediate treatment had been instituted. One year before operation, the nipple was described as red and raw, and there was a bloody and purulent discharge. At that time, the nipple was large and prominent like that on the other breast; then it became less prominent and depressed, but there were no definite nodules in the breast.

The more I study this group, the more I feel that in those cases of Paget's disease which have their onset in the red, finely granular, weep-

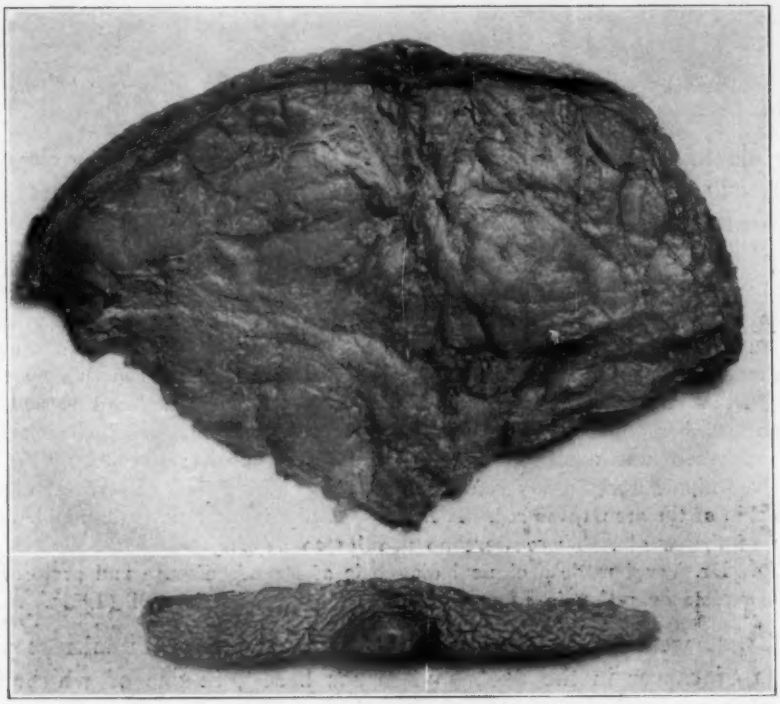

Fig. 22 (Case 11).—Below: Nipple and surrounding areola. The nipple is more retracted than in Figure 17. Above: The dilated ducts in the nipple and the breast beneath. The ducts contain cancer nests. See Figures 20 and 21.

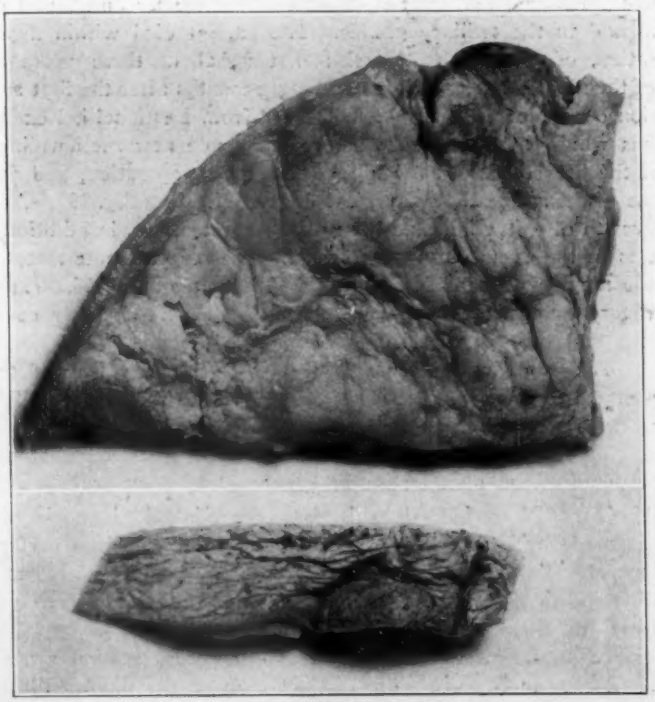

Fig. 23 (Case 12).—Below: The top of the depressed nipple, showing superficial ulceration. Above: Section through nipple and breast. The minute ducts contain cancer nests.

ing nipple the lesion can be shielded in the first few weeks by cleanliness and protection, and, as I have reported, I have two cases to prove this.

CASE 13.—The diagnosis in this case was made from a frozen section by Dr. Lambert, and the complete operation performed by Dr. Verdi in New Haven, Conn. The section from the nipple is typical of Paget cancer (Fig. 20), and the ducts beneath show cancer, as in Figure 21. There is no evidence of cancer in the breast outside the ducts or in the glands. A section sent me by Dr. Lambert is from a senile, fatty breast. The patient, aged 54, had had no trouble in nursing her children. Fifteen months before operation, the nipple became red and there was a slight discharge, with pain, burning and itching. The involved nipple was slightly retracted, and was covered by a superficial ulcer. The skin of the areola was red. There was definite induration of the nipple and skin of the areola. There were no nodules to be palpated in the breast or axilla. Dr. Verdi made a clinical diagnosis of Paget's disease and performed the complete operation in January, 1922, and the patient is well (1923).

There were four cases of cancer of the nipple with microscopic areas of cancer in the ducts and in the breast, in one of which, in addition, the glands showed metastasis.

CASE 14.—This case teaches us the danger of excision of only the nipple for Paget's cancer. The operation was performed in 1906 at Johns Hopkins Hospital, and the sections were carefully studied and diagnosed benign. Less than two years after this operation, Dr. Bastianelli of Rome, Italy, wrote me that he had performed the complete operation for cancer and found cancer in the breast and in the axillary glands. The patient died within a year after this operation, of cerebral metastasis; that is, about three years after the excision of the nipple and three years and eight months after the first appearance of the lesion on the left nipple. When I heard from Bastianelli, I examined the old sections which I had not seen before and made new sections including a portion of the breast beneath the nipple removed at operation, and found that the sections of the nipple showed typical Paget's disease (Fig. 19). Apparently, this overgrowth of epithelium had been misinterpreted, but, in addition, I found cancer nests in the ducts and in the breast. The original note states that the ulcer of the nipple was considered benign. The patient was 55. There was a definite history of cracked nipples with each lactation—the only case in this group which gave this history. The trouble began with an erosion and scab formation. The superficial ulcer was treated with radium, with temporary improvement. The ulcer was tender. The nipple was excised with a good margin of skin and underlying breast. The nipple was prominent, the ulcer superficial and small. The section of the ulcer resembled that shown in Figure 19, the involved ducts those in Figure 21.

CASE 15 (Figs. 24 to 28).—In this case, the clinical diagnosis of Paget's disease was made by Dr. William A. Fisher of Baltimore, who performed the complete operation in June, 1922, and as the axillary glands showed metastasis, postoperative roentgen-ray treatment is being given. It is now one year since the operation and there is no sign of recurrence.

The surface appearance of the nipple and its gross section are shown in Figure 24. The ulcer is much more distinct than on the nipples illustrated in

Figures 17, 22 and 23, and the ducts in the nipple are but slightly enlarged. No gross evidence of cancer could be made out in the breast. The microscopic section of the ulcer on the nipple (Fig. 25) is distinctly cancer, and the cells are of the Paget type. It should be compared with all the other microscopic sections. It shows even more infiltration than is shown in Figure 15, and even in this section, down toward the left, cancer areas can be seen in the ducts.

The study of the involvement of cancer infiltrating the ducts is beautifully illustrated in Figures 26, 27 and 23, the last, a high power photomicrograph,

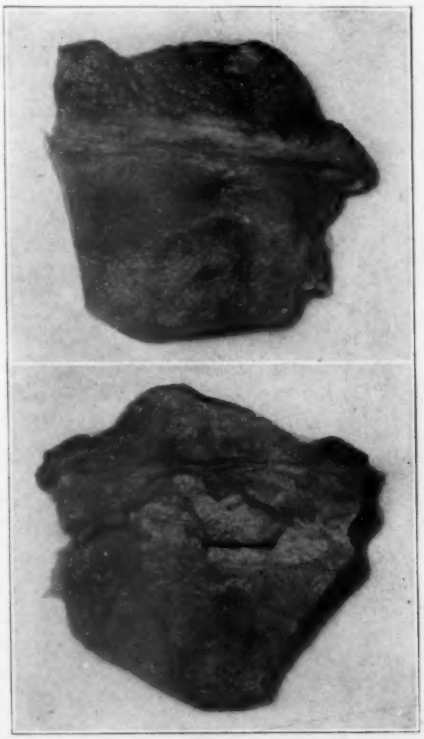

Fig. 24 (Case 15).—Above: The surface of the nipple, the superficial ulcer and scab on top, the zone of thickened epidermis about it and some of the breast beneath may be seen. Below: A section through the nipple and the ulcer. For section of ulcer, see Figure 25; for involved ducts, Figures 26, 27 and 28.

shows that the cancer cells in the duct are of the same morphology (compare with Figure 20).

From numerous sections, there is every evidence that the cancer of the duct is a direct downgrowth from the nipple. Of course, the cells could get mixed in the duct secretion and be carried mechanically. How the cancer cells get into the little lymphatics, I have been unable

to demonstrate. It seems to me there is just as much evidence that the cells are carried there in the lymph stream, as that they reach there by direct continuous growth. However, I have already demonstrated that in Paget's cancer of the nipple you may have metastasis to the glands without clinical gross, and microscopic evidence of any cancer in the ducts or breast. This, to repeat, is the evidence that the operations in cancer of the nipple should always be complete.

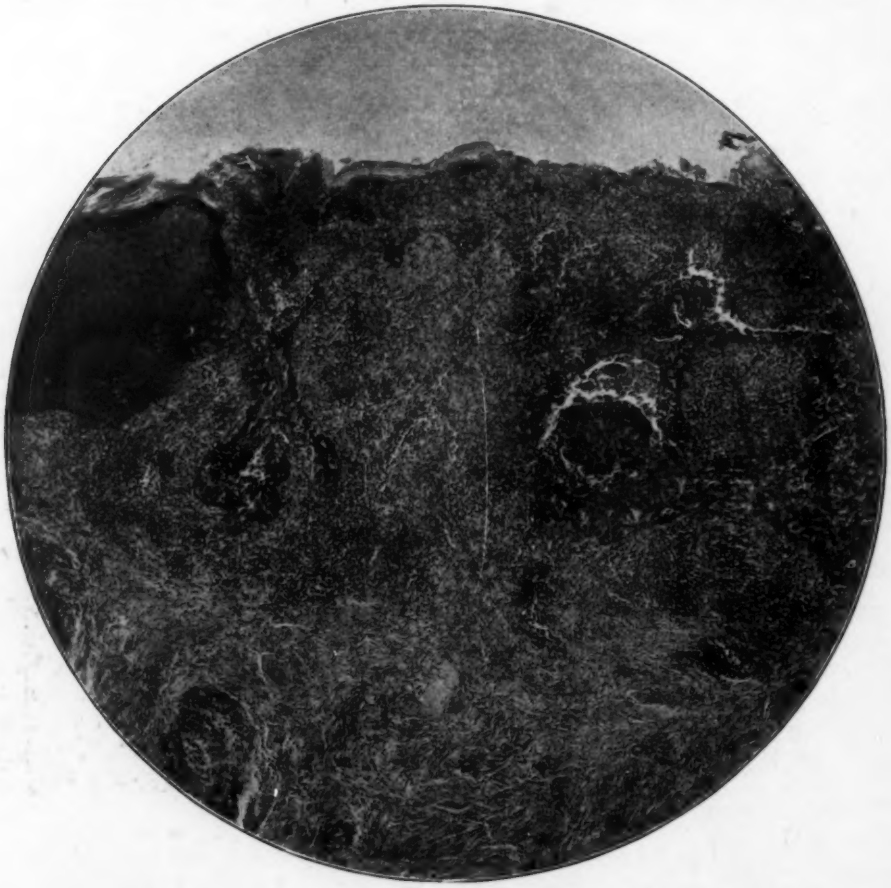

Fig. 25 (Case 15).—Paget's cancer of the nipple. For gross appearance, see Figure 24.

This case of Dr. Fisher is of additional interest as it suggests that this cancer began in a wart, which had been on the nipple for ten years. During this time, it could easily have been treated or removed. For six months, there had been a known ulcer covered with a scab, as shown in Figure 24.

Case 16 (Fig. 29).—This observation in the Johns Hopkins Hospital in 1910 is of interest because, although cancer could not be felt in the breast, it

could be seen on the gross section (Fig. 29), which shows beautifully the appearance of the superficial ulcer of the nipple. The ulcer is not always red, and the nipple may be red without ulceration. Therefore, redness itself is a sign neither of ulcer nor of cancer. My observations show that one must have an ulcer, and a demonstrable ulcer, to have a cancer of the nipple. Yet, one may have ulcer, as I have shown in two cases, without having cancer. The gross section through the nipple and breast shown in Figure 29 pictures the cancer to the left.

Of course, in a case like this, the cancer in the breast could have been primary and that in the nipple secondary, and this has led to a

Fig. 26 (Case 15).—Entire section through nipple shown in Figure 24. The Paget's cancer of the epidermis is shown between the arrows. The zone of cancer is superficial. The dilated duct beneath is filled with cancer cells. See Figure 27.

controversy as to whether the disease of the nipple described by Paget is really primary as concluded by Paget from his clinical studies of late cases. I am rather inclined to the view that the discussion has continued with advocates on both sides, because all have been dealing with late cases. As far as my investigation has gone, no one has published such a large series of early cases as it has been my good fortune to observe, owing entirely to the educational movement.

This patient, aged 69, stated that she first observed on the nipple, two years previously, a pimple on which later a scab formed. Slowly, the ulcer (Fig. 29) developed, and the nipple became partly destroyed. The patient had not felt a tumor in the breast, nor could we feel a tumor in the breast. Dr. Halsted diagnosed the condition Paget's disease and performed the complete operation

Fig. 27 (Case 15).—Cancer infiltrating a duct in case shown in Figure 24. For high power, see Figure 28.

for cancer, in 1910. I found definite Paget cancer in the nipple, in the ducts and in the breast, but not in the glands, and in looking over my old notes I find that I read Paget's article at that time and most of the literature and made this coment: "For practical purposes, I should advise that every case of chronic eczema with ulceration of the nipple in a woman at the cancer age

should be treated as cancer, even though no tumor can be palpated in the breast, unless the appearance of the ulcer, or the presence of other distinct lesions allows a positive diagnosis of syphilis."

The patient died two years later of internal metastasis without local recurrence. We know that a cancer of the breast without metastasis to the axilla offers only about 70 per cent. chances of a cure.

CASE 17.—This case is of interest to me, because it is the first case of Paget's disease observed in the Johns Hopkins surgical clinic in 1903; and, in spite

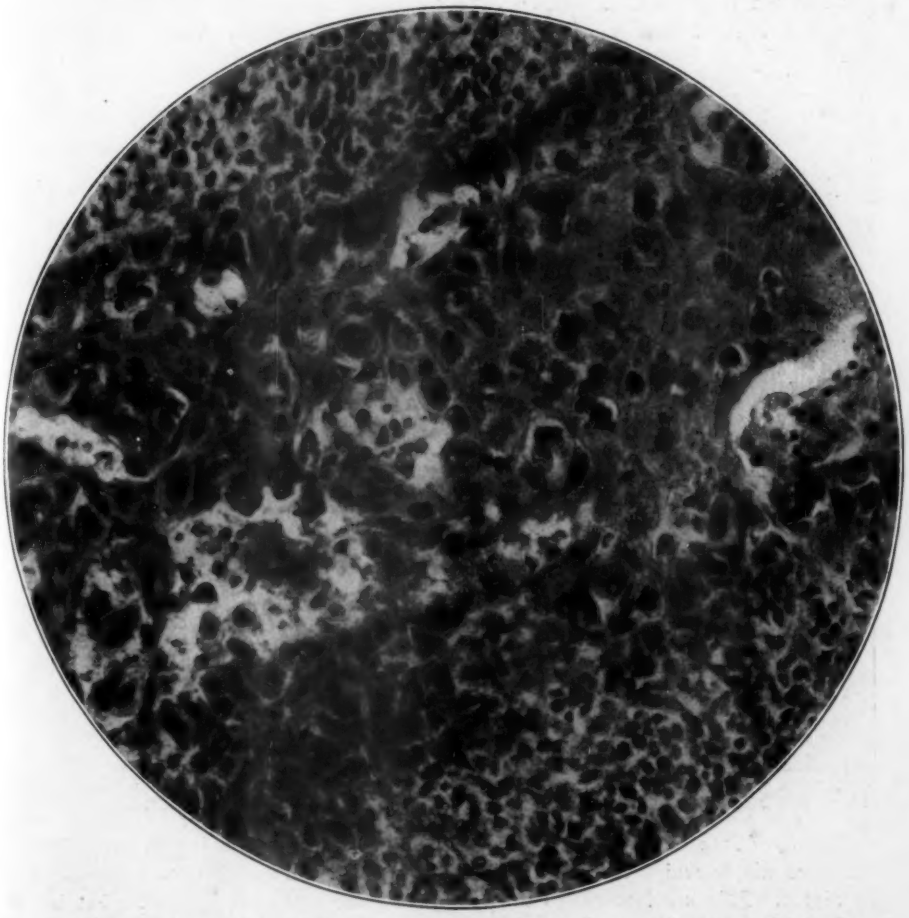

Fig. 28 (Case 15).—High power of cancer in duct showing cells of the Paget type from an area in Figure 27. Compare the morphology of these cells in the duct with Figure 20.

of the fact that nothing could be palpated in the breast, Dr. Finney made the diagnosis of Paget's disease and performed the complete operation for cancer. None of us had seen a case of Paget's disease before this date. This patient died about three years later of cancer of the uterus, without signs of local recurrence or internal metastasis.

The patient, a white woman, aged 49, unmarried, had been aware of a sore nipple for three years. She first spoke of scabs, which would drop off, but

there was no mention of weeping. The examination (by Dr. Follis) revealed that the involved nipple was prominent and red and was more indurated than normal, and its surface was rough, with some weeping. There were no changes in the areola and no masses in the breast.

I described the fresh specimen as follows: "The nipple gives the impression of being depressed or partially destroyed. On top, the epidermis is lost and there is a superficial ulcer. The surrounding epidermis of the nipple is hypertrophied. The surface of the ulcer is red and finely granular. On section through the nipple and breast no cancer can be made out in the breast, but the nipple is infiltrated by a distinct new growth of a finely granular appearance.

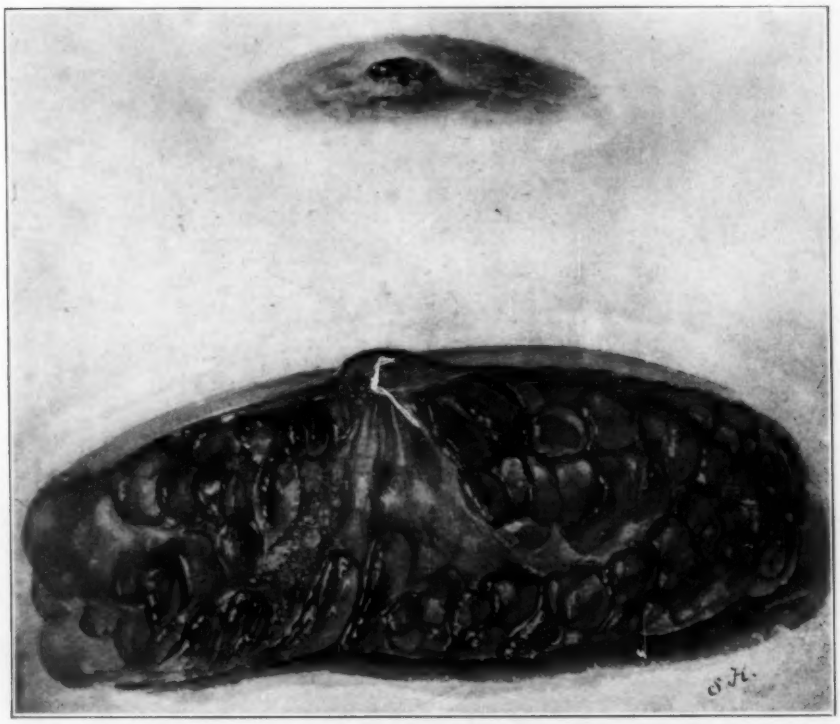

Fig. 29 (Case 16).—Fresh specimen, showing the ulcerated and partially destroyed nipple and the gross involvement of the breast with cancer beneath the nipple. This involvement of the breast was not made out clinically, but is confirmed by the microscopic section.

The sections were typical of Paget's cancer of the nipple, and cancer was found in the ducts and in the breast in minute areas, but not in the glands.

Of course, at that time I did not know the typical microscopic appearance of Paget's cancer of the nipple, but there was no difficulty in recognizing that the lesion of the nipple was a carcinoma. We described it then as an epithelioma.

Following are three cases presenting the later stage of Paget's cancer of the nipple, in which the nipple is replaced by an ulcer, but in which as yet there is no palpable mass in the breast.

These three cases differ from the previous ten in that the nipple was completely destroyed and replaced by an ulcer covered with a scab. This ulcer resembled the ordinary basal-cell cancer of the skin clinically, but the sections showed a superficial growth identical with the microscopic picture in the previous ten cases, a picture entirely different from basal-cell or spinal-cell cancer of the skin. The study of these three cases also shows a condition which Paget never observed. He wrote that he had never seen the ulcer extending beyond the areola.

Fig. 30 (Case 18).—Superficial ulcer which has destroyed the nipple and involved the areola. For microscopic section, see Figure 31.

In one of our cases (Fig. 32), the ulcer was shown to extend beyond the areola, and in the other (Fig. 35) the superficial ulceration with scab formation covered almost the entire breast.

The duration of the nipple lesion in two cases was five years. In both, cancer was found in the ducts, but not in the breast outside the ducts, and in only one case were the glands involved. In one case, the duration of the nipple lesion was one year. Infiltration of the cancer cells into the ducts was clearly shown in the section. There was no involvement of the breast outside the ducts, nor of the axillary glands. One of these patients lived five years and died of influenzal pneumonia;

the second is living today, three years after operation, and the third, the one in which the axillary glands showed metastasis, has failed to answer inquiries.

Case 18 (Fig. 30).—This case is of especial interest, because the patient was aware of a wart on each nipple for many years. Neither wart had ever bled or given any trouble. The wart on the right nipple resembled that pictured in Figure 5, except that it was larger. One year before operation, a trauma

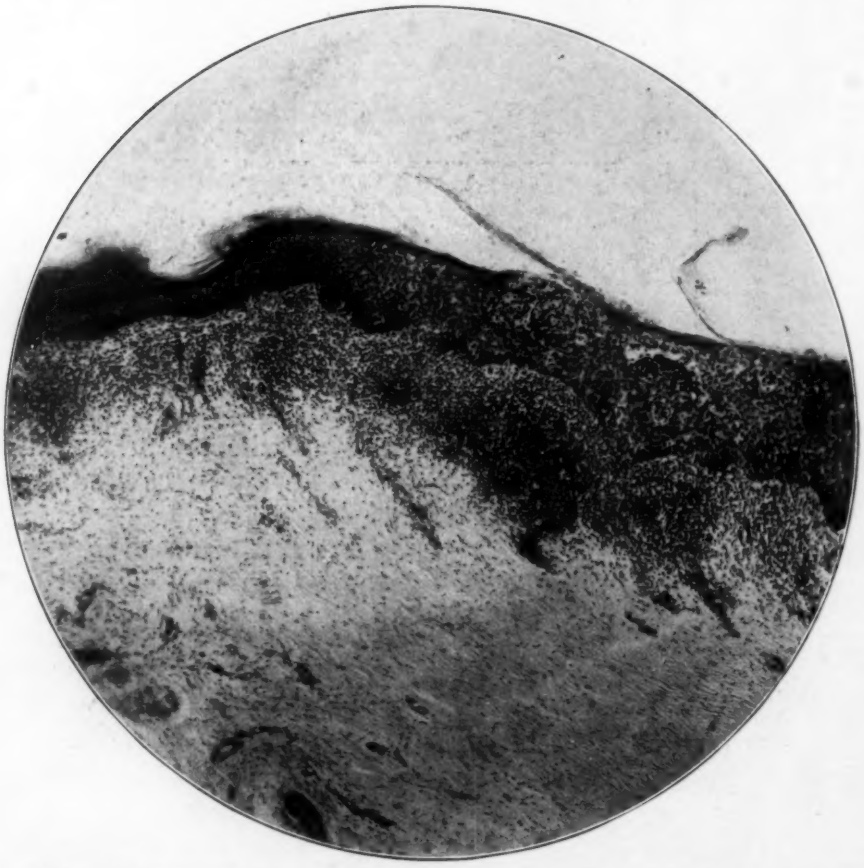

Fig. 31 (Case 18).—Paget's cancer-ulcer of the nipple. For gross section see Figure 30. Compare with Figures 14, 15, 19 and 26.

knocked off the wart on the left nipple, and apparently the wound never healed. A crust formed, and gradually the area of ulceration enlarged until it assumed the appearance shown in Figure 30. The nipple was destroyed; there was a superficial ulcer covered with a crust, like an ordinary basal-cell cancer of the skin; there was very little induration about the ulcer, and no palpable mass could be felt in the breast and axilla. The patient was 74 years of age and unmarried.

I performed the complete operation for cancer in June, 1917. The apparently innocent wart on the right nipple was treated daily with soap and water and covered with petrolatum, and completely disappeared in a few months. It is therefore fair to assume that this woman could have been protected from cancer if the warts on both nipples had received the same treatment before the injury to the nipple took place, and it is not unlikely that the proper dressing and protection of the little innocent wound in the first days or weeks after the injury would have prevented the later development of cancer in the unhealed ulcer.

On section, the ulcer was but a few millimeters in thickness, and there was no involvement of the breast beneath to be seen with the naked eye. The

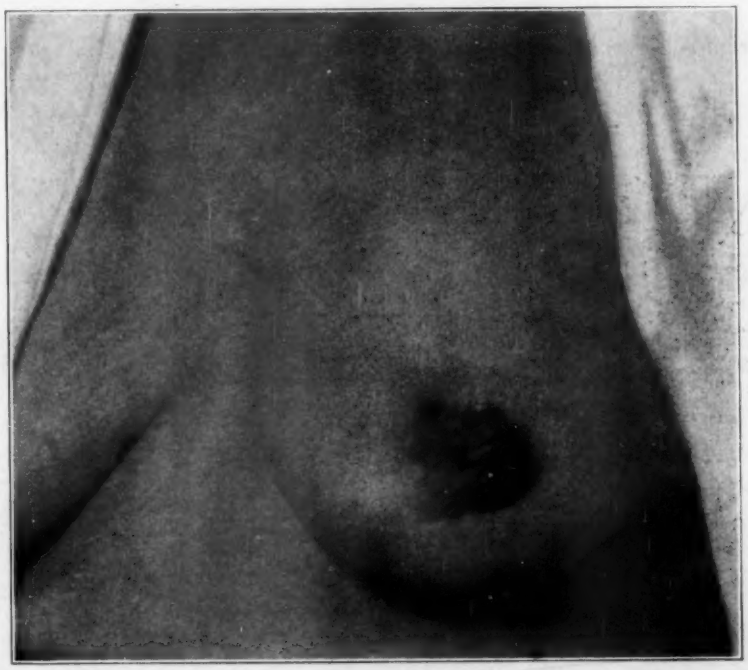

Fig. 32 (Case 19).—Superficial ulcer which has destroyed the nipple, covered the areola and invaded the skin of the breast. For microscopic appearance of ulcer, see Figure 33.

section through the ulcer (Fig. 31) shows a Paget's cancer, and in the lymphoid-cell reaction beneath the epidermal zone of cancer, there are cancer nests. Cancer nests were also found in a few ducts, but not in the breast or in the axilla.

As I have already stated, this patient died five years later of influenzal pneumonia.

Case 19 (Fig. 32, 33 and 34).—The clinical picture of the nipple lesion in this case (Fig. 32) differs from that shown in Figure 30 only in that the superficial ulcer with scab formation is larger and has extended over the skin of the breast. This ulcer, microscopically, is a Paget cancer, and the morphology

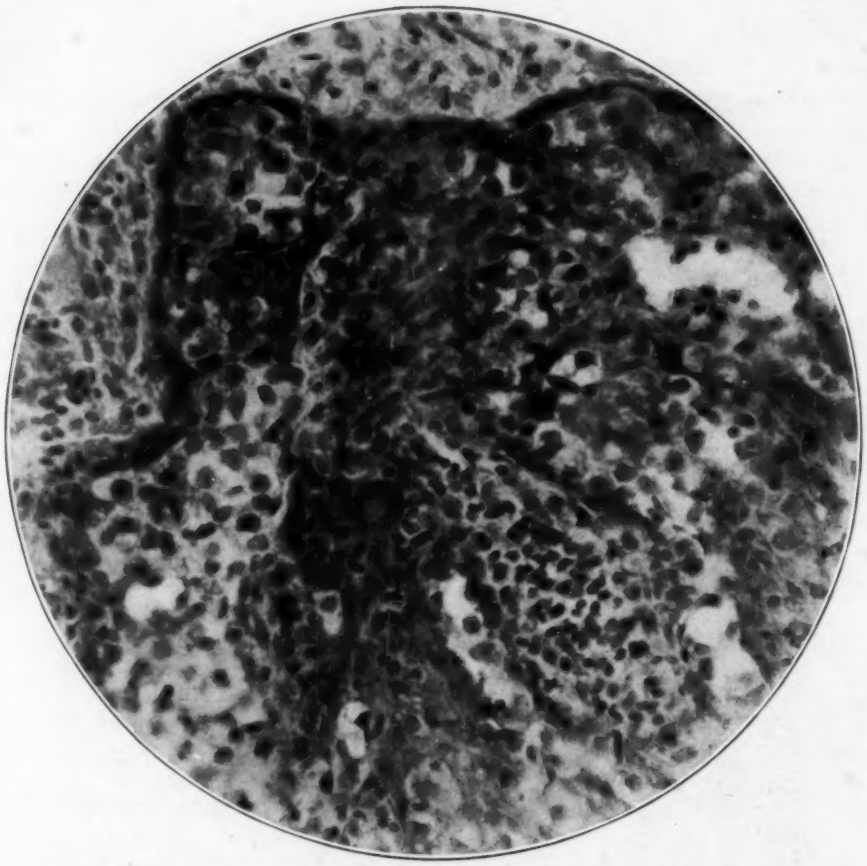

Fig. 33 (Case 19).—High-power of ulcer shown in Figure 32; clearly malignant; definite cells of the Paget type. Compare with Figures 20 and 28.

Fig. 34 (Case 19).—Section through ulcer and breast shown in Figure 32. The ulcer destroying the nipple and involving the areola and surrounding skin is between the arrows. The top zone (very black) is scab formation; the lower zone is cancer. No cancer was found in the breast beneath, except in a few of the dilated ducts. The breast is the seat of chronic cystic mastitis. Grumous material expressed from one duct can be seen at *x*.

of the cells under the high power is shown in Figure 33. In this breast, the ducts beneath the nipple and throughout the breast were unusually dilated (Fig. 34), presenting the picture of chronic cystic mastitis. Yet, no evidence of cancer could be found, except in a few ducts beneath the nipple. There was no involvement of the axillary glands.

The patient, a white woman, aged 58, gave no history of difficulty with the nipple during lactation. She observed fish-scales on the left nipple, five years before operation. Apparently, she paid little attention to it until she found that the nipple had disappeared and that scab and scale formation were extend-

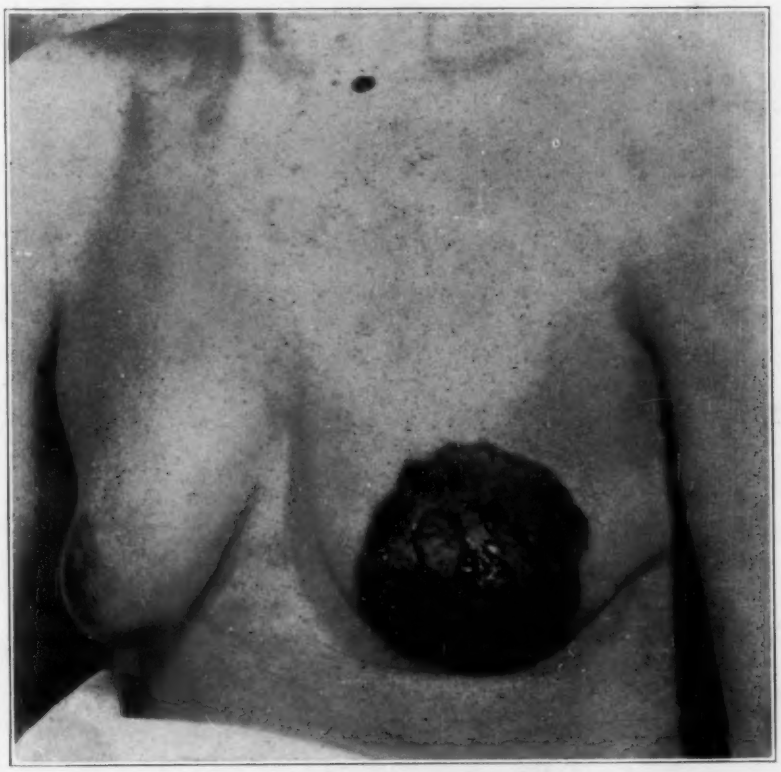

Fig. 35 (Case 20).—The superficial ulcer here differs from that in Figure 32 only in extent. For section through ulcer, see Figure 36.

ing over the skin. Then, for the first time, she sought the advice of a physician. She has been treated with some type of local applications and with violet rays. There has been weeping only when the crusts came off, and discomfort only when the crusts remained on too long. At my examination, nothing could be made out, except what is shown in Figure 32. The ulcer had a very slightly indurated edge.

I performed the complete operation in June, 1920, and today, three years since operation, the patient is in good health. The axillary glands showed no metastasis.

Case 20 (Figs. 35, 36 and 37).—This case is the only example of its kind in my list and so far I have been unable to get a description of its like in the literature.

Figure 35 shows a superficial ulcer covered with a scab practically identical with those shown in Figures 30 and 32. The unusual part is its great extent. Superficial basal-cell cancer of the skin, of this size or larger, I have observed on a few occasions but never on the skin over the breast. The thickness of the epithelial overgrowth is shown in Figure 36, which with the low power does not look unlike an ordinary basal-cell cancer. The base is sharply outlined and in the section shown in Figure 36 no cancer nests can be found in the tissue beneath the base of the superficial cancer. Yet, the ducts beneath in many places are infiltrated (Fig. 37) with cancer cells of the Paget type (compare with Figure 28). With the high power, the morphology of the cells in the growth, shown in Figure 36 is identical with that in our other cases of Paget's cancer (see Figure 20).

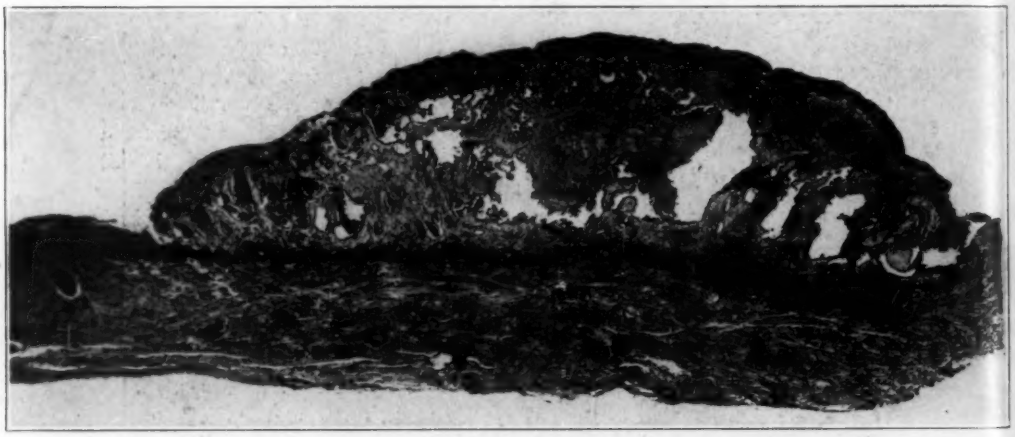

Fig. 36 (Case 20).—The entire section through the ulcer shown in Figure 35. This cancer-ulcer differs from all other cases only in the thickness of the epithelial zone. Compare with Figures 14, 15, 19, 25, 26 and 31.

This patient, a white woman, aged 51, observed, five years before operation, a red pimple on the nipple. A scab formed. Insidiously, the scab formation gradually spread, and the nipple disappeared. There had never been pain or itching, and apparently very little weeping. The woman did not consult her physician until one year ago, and all local treatment had failed to check the spreading of the skin disease. At the examination, there was very little induration, and no mass could be felt in the breast, but the axillary glands were palpable. The diagnosis of Paget's cancer was made by Dr. Reid of Johns Hopkins Hospital, and the complete operation was performed.

At the pathologic examination, we could demonstrate cancer of the ducts and metastasis to the glands, but were unable to find cancer in the breast outside the ducts.

Both the patient and her physician failed to answer the inquiries directed to them.

The end stage of Paget's cancer of the nipple, that first described by Paget, in which, in addition to cancer of the nipple, there is a palpable mass in the breast due to a fully developed carcinoma, is illustrated by three cases.

That I should be able to report but three examples of Paget's disease among twenty-three lesions of the nipple subjected to operation

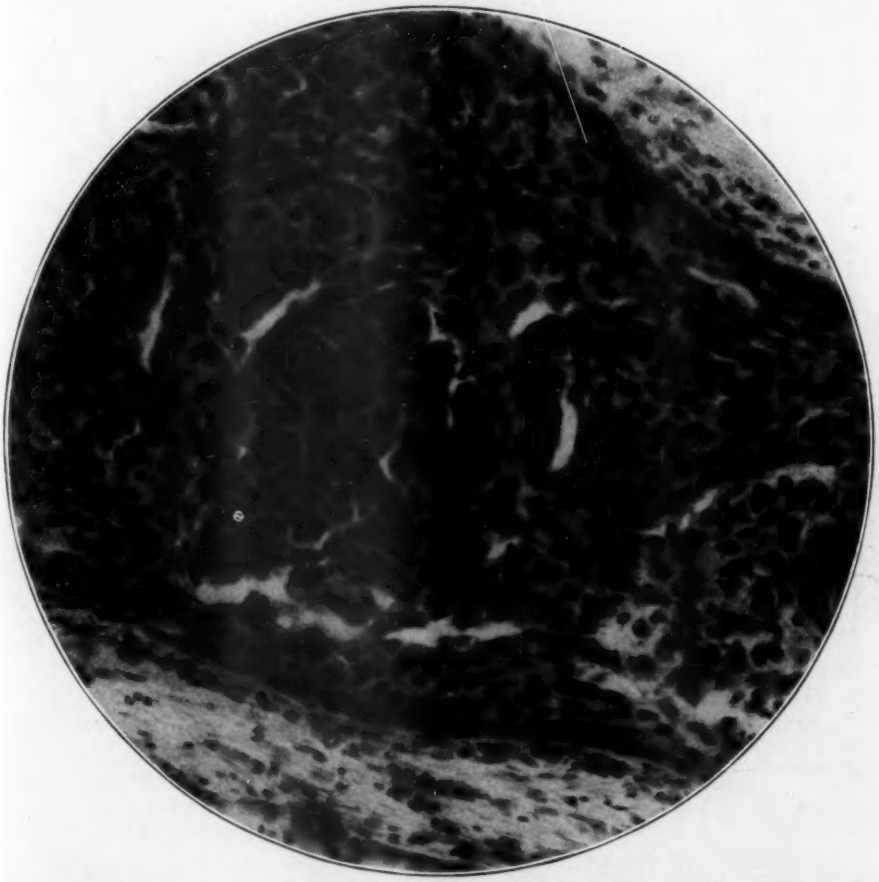

Fig. 37 (Case 20).—High power photomicrograph of cancer of duct in case shown in Figures 35 and 36. The morphology of the cells in the fungus ulcer shown in Figure 36 corresponds with the morphology of the cells in the ducts beneath as illustrated in this Figure 37.

is a definite indication that the women up to 1874 delayed much longer in seeking aid than the women in this country have since 1890. It is important to remember that, among the fifteen cases observed by Paget in which there was a definite cancer of the breast, the duration of the nipple lesion has varied from one to three years. The entire

duration of the nipple lesion in my three cases of fully developed Paget cancer varied from two to five years. Therefore, I have never observed the latest stage of Paget's disease with an interval less than two years. It is interesting to note that, among the ten cases of Paget's disease in the early stage, in which the nipple is not yet destroyed, there are only two cases of two years' or longer duration (two and three years, respectively). Among the three cases of later Paget's disease in which the nipple is destroyed two cases were of five years' duration. Among my seven cases microscopically benign, there is but one of two years' duration. Therefore, in my twenty examples of Paget's disease which had not yet reached the stage described by Paget, the duration of the nipple lesion in seven cases was from two to five years. It seems strange that Paget did not observe and describe them.

Case 21.—Figure 38 shows our first example of the disease described by Paget. In Figure 38, below, the nipple has been destroyed and replaced by a superficial ulcer from which the scab has been removed during the operation. Figure 38, above, the gross section of the breast, shows the ulcer destroying the nipple, and the cancer to the left. Sections demonstrated areas of cancer between the nipple ulcer and the breast cancer.

This case was diagnosed and the complete operation performed by Dr. Omar Pancoast in 1905. I reported it in my chapter on lesions of the female breast in Kelly-Noble's Abdominal Surgery in 1907 as an example of Paget's disease. The diagnosis was based upon the clinical history. The old pathologic report made by me describes a cancer in the ulcer of the nipple, a scirrhous cancer of the breast and nests of cancer in the ducts between the gross cancer and the nipple ulcer; and metastasis to the glands. Unfortunately, the sections have been lost, or exhausted in teaching, so I have been unable to restudy these sections, and am therefore unable to state definitely whether the cells in the cancer of the nipple were of the Paget type.

The clinical history as sent to me recorded that the woman was 55 years of age and unmarried. The lesion of the nipple had been present two and one-half years; her attention was called to it by the blood-stained, purulent secretion. The nipple gradually disappeared and was replaced by an ulcer. The patient noticed a lump in the breast about five months before operation.

We have, therefore, a clinical history as described by Paget.

The patient died within one year after operation, apparently of internal metastasis.

Case 22 (Fig. 39).—This case, from the clinical history, is typical of the disease as described by Paget, and the section of the cancer of the nipple has the morphology of Paget's. The breast was diffusely infiltrated with cancer. The case is rather unique in that the lesion of the nipple dated from a lactation. Figure 39 pictures the excavated ulcer of the nipple and the asymmetry of the breast due to the cancer growth. The axillary glands were extensively involved and, although we have been unable to trace the patient since the operation in 1920, there is every reason to believe that she is not living.

I submitted sections from the ulcer of the nipple in this case to Dr. Kilgore, who had made a very exhaustive study of the cellular pathology of Paget's

disease of the nipple in my laboratory, which he has reported. He agrees with me that the section of the nipple ulcer undoubtedly contains cells of the Paget type.

This history is too long to be given in detail. It shows both neglect by the patient of an evident lesion of the breast, and a mistake on the part of her

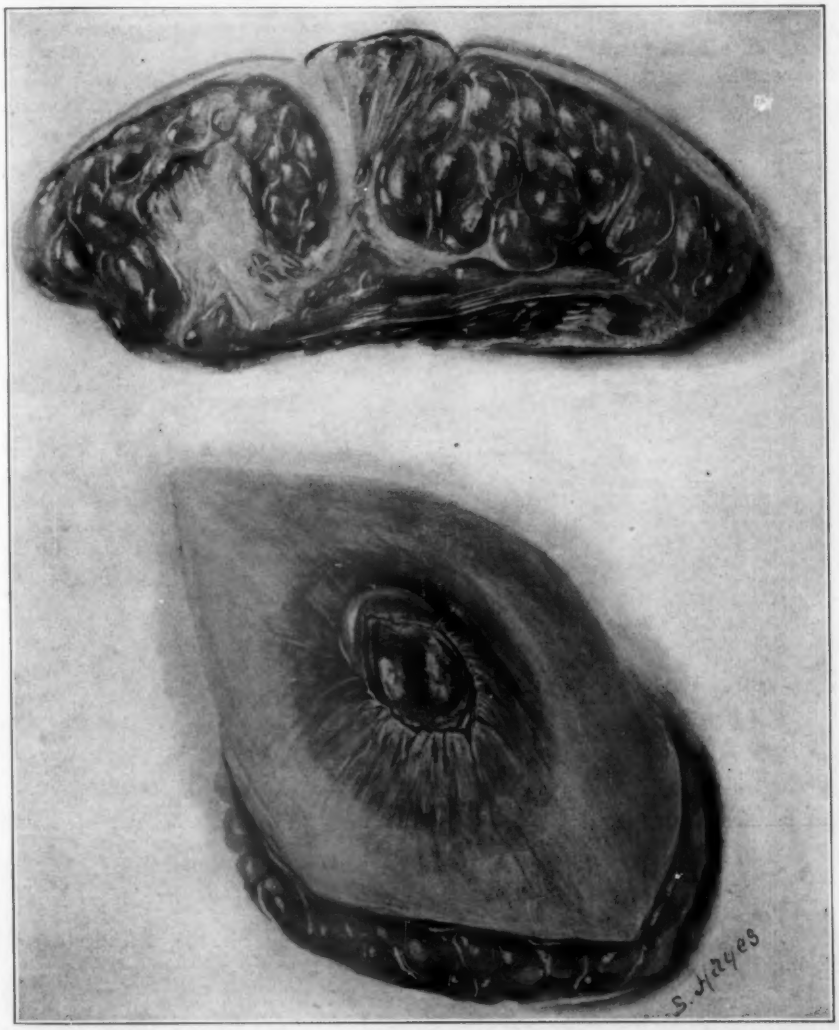

Fig. 38 (Case 21).—Original painting of a cancer of the nipple and the breast corresponding with Paget's original description. Below: The ulcer destroying the nipple; above: section through the ulcerated nipple and breast. The gross cancer is to the left.

physician in not interpreting the picture correctly. It had been diagnosed a benign lesion of lactation, until the evident cancer, shown in Figure 39, brought the patient to the clinic.

Five years before operation, after the incision of a breast abscess during lactation, the nipple became retracted and sore, and had never healed. Apparently, the induration of the abscess never disappeared. Gradually, the nipple was replaced by an ulcer, and subsequent pregnancies made the condition worse. Her last pregnancy was three months before operation. It is impossible to estimate when malignancy began. The only positive evidence of Paget's disease is the definite morphology of the cells in the ulcer of the nipple.

CASE 23.—The diagnosis in this case is purely clinical. The patient came under observation with local and internal metastasis about seven months after the complete operation for a cancer of the breast. She claimed that the lesion of the nipple began two years before this operation, when she was nursing

Fig. 39 (Case 22).—Appearance of right breast; illustrating Paget's cancer of the nipple and breast in its latest stage.

her youngest child. It gradually developed into an ulcer which destroyed the nipple. She was given frequent roentgen-ray treatments, which apparently had no influence on the ulcer and scab formation. When the operation was performed, there was a definite lump in the breast. The glands showed metastasis.

LITERATURE

Kilgore [1] gives all the recent references to the literature. His paper is chiefly devoted to a microscopic study of the material in my labora-

1. Kilgore, A. R.: Is Paget's Disease of the Nipple Primary or Secondary to Cancer of the Underlying Breast? Arch. Surg. **3**:324 (Sept.) 1921.

tory. His conclusions that the disease is primary in the nipple are in agreement with mine.

Handley in the recent second edition of his book on cancer of the breast has introduced a very complete chapter on Paget's disease, with full extracts from Paget's first contribution.

McFarland in the book on the breast which he wrote with Deaver, gives a complete bibliography. For this reason, discussion of the literature seems unnecessary.

My problem has been somewhat different from all the others. It, however, is suggested in Paget's first contribution: 1. To give the evidence, if it is there, that cancer of the nipple is a preventable disease; to teach the general profession what information to give their patients in order to save them from death from cancer of the breast. It seems to me that this is clear: If a woman over twenty years of age feels a lump in the breast, or observes any change in the nipple, she should consult her physician the next day. 2. Clearly to teach the medical profession what to do when there is a lesion of the nipple in its various stages and degrees. This I have attempted as far as the experience of the thirty cases allowed.

CONGENITAL DEFICIENCY OF THE DIAPHRAGM *

ELLIOTT C. CUTLER, M.D.
AND
HENRY S. F. COOPER, A.B.
BOSTON

The recent and considerable increase in our knowledge of diaphragmatic hernia has been due in a large part to information acquired during routine roentgen-ray studies of the gastro-intestinal tract (Bevan,[1] Giffin,[2] Howk and Herring [3]). It has been shown by the roentgen ray, following an opaque meal, that patients reporting with vague epigastric or indigestional complaints may have either the stomach or intestines or both in the thoracic cavity. These studies have demonstrated that the thoracic contents may vary with the position of the patient, indicating a fairly wide defect in the abdominothoracic partition. More often they have shown that a portion of the stomach alone is involved in the hernia, which would seem to indicate that the defect lies at the esophageal opening (Bevan,[1] Borden,[4] Frank,[5] Hume [6]). A further stimulus to our knowledge of this condition was brought about through the study and treatment of the enormous number of traumatic injuries to the diaphragm during the recent European war. The acute and late sequelae to such injuries gave rise to numberless imperative operations, and the experience thus obtained has greatly furthered our ability to cope with the more rare and less urgent types of defects in the diaphragm encountered in civil life.

It is true that in the type of case usually encountered in civil life, except for the extremely rare cases of either destructive or inflammatory

---

* From the Laboratory of Surgical Research, Harvard Medical School.

1. Bevan, A. D.: Diaphragmatic Hernia, Arch. Surg. **1**:23-37 (July) 1920.

2. Giffin, H. Z.: The Diagnosis of Diaphragmatic Hernia, Ann. Surg. **55**: 388-399, 1912.

3. Howk, H. J., and Herring, J. A.: A Case of Diaphragmatic Hernia Without Severe Symptoms Discovered in Routine X-Ray Examination of Chest, Am. J. Roentgenol. **7**:247-249 (May) 1920.

4. Borden, D. L.: Diaphragmatic Hernia, Ann. Surg. **75**:337-344 (March) 1922.

5. Frank, Louis: Congenital Diaphragmatic Hernia, Ann. Surg. **71**:280-282 (March) 1920.

6. Hume, J. B.: Congenital Diaphragmatic Hernia, Brit. J. Surg. **10**:207-215 (Oct.) 1922.

lesions in the herniated intestine (Bell,[7] Caffee,[8] Hawkes,[9] Meyer,[10] Moppert[11]), immediate operative intervention is not necessary. However, there can be no doubt that a large number of obscure cases of indigestion, biliousness, and epigastric discomfort may be due to such an anatomic lesion,[12] and it behooves us to enlarge our understanding of these defects with every opportunity. The finding of an unusual type of this malady, although in a dog, may therefore be of some value.

Considered broadly, there are the following classes of congenital lesions of the diaphragm: (1) true hernia with a sac covering the displaced gut; (2) false hernia, or hernia without a sac, and (3) eventration.

The true congenital hernia with a sac is due to a weak spot in the diaphragm, which gives way under the strain of increased abdominal pressure created by the growth of the viscera and forms a sac protruding into the thorax and containing the herniated organs. It is obvious that such a lesion must develop after the diaphragm has been formed. This type has been termed by Williams[13] "congenital" as opposed to the false hernia, which he has termed "embryonic." The latter type is caused by a defect in the formation of the diaphragm, which leaves an opening between the thorax and abdomen through which the viscera protrude without a covering sac. Since the diaphragm completely separates the pleural and peritoneal cavities in the 20 mm. embryo, such a lesion must occur very early in intra-uterine life. This type is probably more common than the true hernia, and Hume[6] of London and Latta[14] of Omaha have recently elaborated the embryologic failure that results in this lesion. Latta collected from the literature 127 cases of false or spurious hernia of the diaphragm, and classifies them more properly as congenital deficiency of the diaphragm.

---

7. Bell, E. T.: Diaphragmatic Hernia, Am. J. M. Sc. **137**:581-584, N. S., 1909.

8. Caffee, B. V.: A Case of Incarcerated and Obstructed Diaphragmatic Hernia with Operation and Recovery, J. A. M. A. **57**:20 (July) 1911.

9. Hawkes, C. E.: Report of a Case of Strangulated Diaphragmatic Hernia with Operation and Recovery, J. A. M. A. **68**:369 (Feb. 3) 1917.

10. Meyer, A. W.: A Case of True Congenital Diaphragmatic Hernia Complicated by Volvulus of the Stomach in a Woman Aged 53, J. Anat. & Physiol. **48**:153-160, 1913-1914.

11. Moppert, G. G.: Gangrenous Perforation of the Stomach, a Complication of Diaphragmatic Hernia, J. de chir. **20**:453-463 (Nov.) 1922; Internat. Abstr. Surg. **34**:172, 1923.

12. Seibert, O. J.: Diaphragmatic Hernia, Surg., Gynec. & Obst. **23**:465-468 (Oct.) 1916.

13. Williams, H. O.: A Case of Diaphramatic Hernia, Lancet **1**:931, 1908.

14. Latta, J. S.: Congenital Deficiency of the Diaphragm, Am. J. Dis. Child. **24**:297-305 (Oct.) 1922.

Eventration of the diaphragm (Aronson,[15] Bayne-Jones,[16] Jaffin,[17] Korns,[18] Lerche,[19] Sailer and Rhein,[20] Stein [21]) is a condition in which one or both domes may consist of only a thin fibrous structure and often of nothing more than pleura and peritoneum without muscular elements. This condition may be present on both sides, and when it occurs, the diaphragm plays no part in respiration but remains as a thin dome-shaped fibrous structure that may reach as high as the second or third rib. This is a very rare condition, only forty-five cases having been reported in the literature. The congenital form is probably due to failure of development of the muscular elements of the diaphragm or of the phrenic nerve, both of which structures descend from the region of the fifth cervical somite early in embryonic development. The acquired type occurs both as a complication in some acute infections and following trauma to the neck in which the phrenic nerve has been involved.

The embryologic development of the diaphragm is of much interest with regard to the types of hernia, both false and true, that have been identified pathologically and clinically. Apparently, this structure has four different sources: (1) the septum transversum; (2) the primitive mesentery; (3) the pleuroperitoneal and pleuropericardial membranes, and (4) portions of the wall of the coelomic cavity (Fig. 1).

The mesenchyme of the ventral mesentery which carries the omphalomesenteric veins to the heart gives rise to the septum transversum. The liver develops in the inferior aspect of this septum from cells that bud off from the alimentary canal (entoderm). This septum is first seen to be differentiated in the 2 mm. human embryo. It spreads out fanlike and is attached to the body wall ventrally and ventrolaterally, providing a shelf for the heart to rest on. The ventral portion of the pleuropericardial cavity is thus partitioned off from the abdominal cavity,

---

15. Aronson, E. A.: Eventration of Right Half of the Diaphragm, Med. Rec. **93**:37, 1918.

16. Bayne-Jones: Eventration of the Diaphragm and Report of Right-Sided Eventration, Arch. Int. Med. **17**:221 (Feb.) 1916.

17. Jaffin, A. E., and Honeij, J. A.: Eventration of the Diaphragm, Boston M. & S. J. **188**:593-596 (April 19) 1923.

18. Korns, H. M.: The Diagnosis of Eventration of the Diaphragm with Report of a Case of Aplasia of the Right Lung and Right Half of the Diaphragm, Associated with Congenital Dextrocardia, Arch. Int. Med. **28**:192-212 (Aug.) 1921.

19. Lerche, W.: Insufficiency of the Diaphragm, with the Report of a Case and the Surgical Treatment Thereof, Surg., Gynec. & Obst. **34**:224-229 (Feb.) 1922.

20. Sailer and Rhein: Eventration of the Diaphragm, and Report of a Case, Am. J. Med. Sc. **129**:688, 1905.

21. Stein, I. F.: Eventration of the Diaphragm, with the Report of a Typical Case with X-Ray Diagnosis, Surg., Gynec. & Obst. **18**:547-550, 1914.

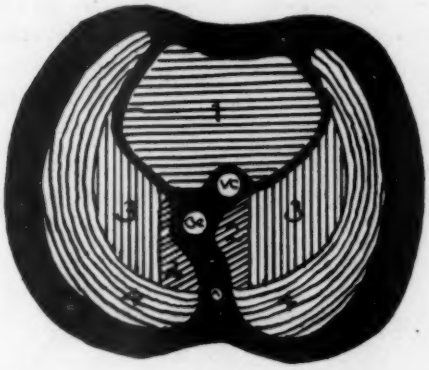

Fig. 1.—Schematic drawing of diaphragm (after Broman) to show positions of the various contributing elements; *1*, portion derived from the septum transversum; *2*, *2*, derivatives of the primitive mesentery; *3*, *3*, derivatives of the pleuroperitoneal membranes; *4*, *4*, portions derived from the body wall; *a*, aorta; *oe*, esophagus; *vc*, vena cava.

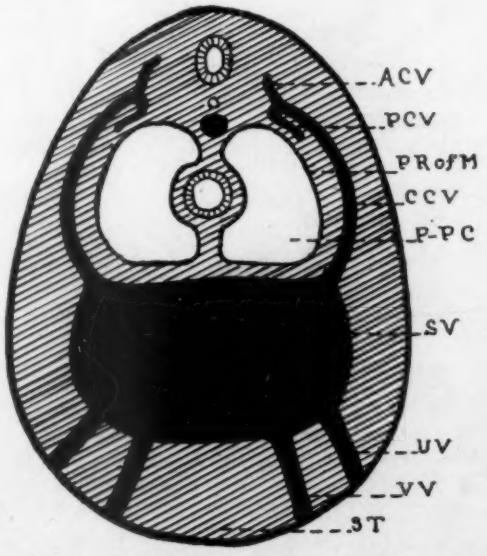

Fig. 2.—Schematic drawing of the cross-section of a 2.5 mm. human embryo, showing the relation of the structures that go to make up the diaphragm; *acv*, anterior cardinal vein; *pcv*, posterior cardinal vein; *pr*, of *M*, pulmonary ridge of Mall; *ccv*, common cardinal vein; *ppc*, pleuroperitoneal canal; *sv*, sinus venosus; *uv*, umbilical vein; *vv*, vitelline vein; *st*, septum transversum.

while the dorsal portion remains open as the paired pleuroperitoneal canals, the latter being separated by the primitive mesentery. In the 2 mm. embryo, the dorsal limit of the septum transversum is opposite the second cervical somite. As the embryo develops, this relation is altered until, at 20 mm., the dorsal limit is opposite the twelfth thoracic somite, having descended nineteen somites and reached its permanent position.

The pleuroperitoneal and pleuropericardial membranes have their origin in a vertical ridge of mesenchyme (the pulmonary ridge of

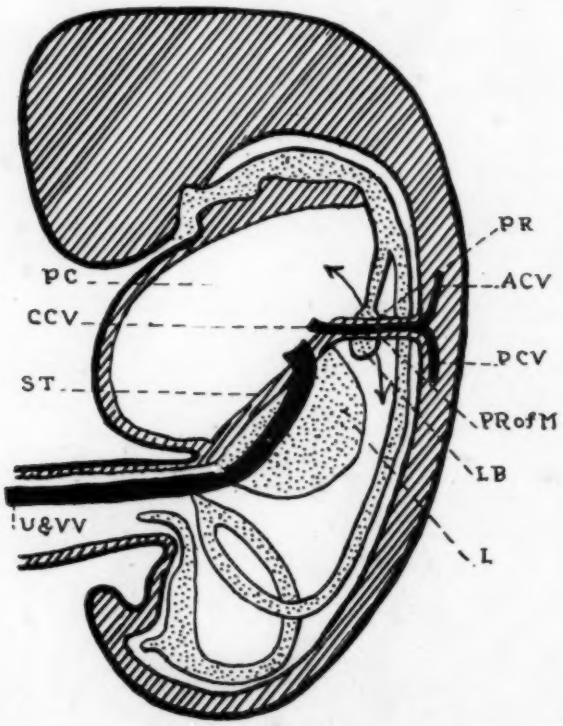

Fig. 3.—Diagrammatic view of a sagittal section of a human embryo of about 7 mm., showing the relation of the structures that go to make up the diaphragm; *pc*, pleural cavity; *ccv*, common cardinal vein; *st*, septum transversum; *u & vv*, umbilical and vitelline veins; *pr*, pulmonary ridge; *acv*, anterior cardinal vein; *pcv*, posterior cardinal vein; *pr* of *M*, pulmonary ridge of Mall; *lb*, lung bud; *l*, liver.

Mall), which carries the common cardinal veins from the dorsolateral aspects of the body cavity to the septum transversum and heart (Fig. 2). At 7 mm., this ridge is first seen bulging into the dorsolateral aspects of the pleuroperitoneal canals at the point occupied by the lung buds. The cephalad border of the ridge remains fixed, while the caudad border is

carried down with the septum transversum in its descent until it reaches a point below the lower pole of the lung. Thus, the pulmonary ridge becomes a triangular membrane, its base attached to the dorsal body wall, its apex continuous with the septum transversum (Figs. 3 and 4). The cephalad border, the pleuropericardial membrane, grows around the upper portion of the lung bud, separates it from the heart and forms the pericardium. The caudad border, the pleuroperitoneal membrane, grows around the lower pole of the lung bud, fuses with the mesonephros dorsolaterally and the mesentery medially, and practically closes

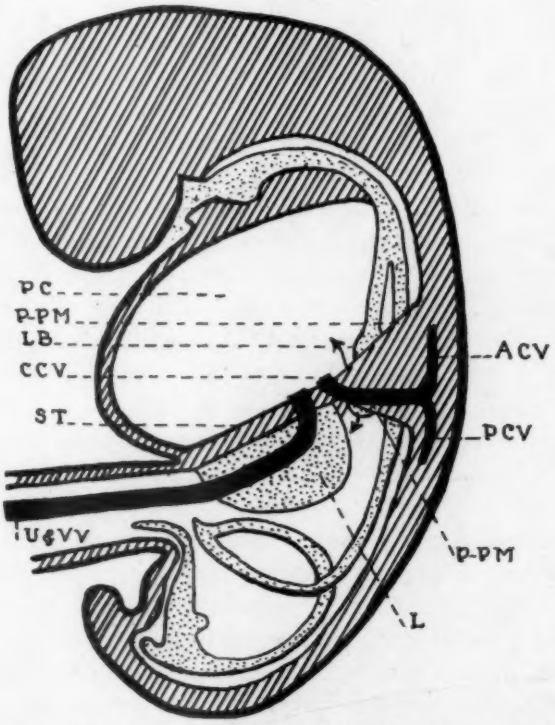

Fig. 4.—Diagrammatic view of a sagittal section of a human embryo of about 9 mm., showing the spreading of the pulmonary ridge with the descent of the diaphragm; *ppm*, pleuropericardial membrane; other letters as in Figure 3.

the pleuroperitoneal canal, leaving only a slit at its dorsomedial aspect (the pleuroperitoneal hiatus). This state of affairs exists in the 11 mm. embryo. The pleuroperitoneal hiatus is finally closed by the growth of the primitive mesentery, and the diaphragm is fully formed when the embryo has attained a length of 20 mm. As growth continues and the diameter of the body cavity increases with relation to that of the heart, the diaphragm is added to by mesenchyme incorporated from

the walls of the coelom. Thus, the diaphragm has four sources: its ventral pericardial portion is formed from (1) the septum transversum; its lateral portion from (2) the pleuroperitoneal membranes plus (3) derivatives from the body wall, and the medial, dorsal portion from (4) the primitive mesentery. Its muscular portion comes from a pair of premuscle masses which, in the 9 mm. embryo, lie one on each side of the fifth cervical somite. This muscle mass goes caudad with the septum transversum, carrying the phrenic nerve with it, and develops chiefly in the dorsal portion of the diaphragm.

To one unaccustomed to the study of embryologic transverse and sagittal sections, the tracing of this development is difficult. However, if one remembers that the septum transversum begins at the ventral mesentery; that the heart develops as a coiled tube on its cephalad aspect; that the lung is a budding off from the gut as it pushes downward, and that the cardinal veins pass on the lateral walls while the wolffian body descends behind, it is possible to appreciate the explanations given. The liver develops directly in the inferior aspect of the septum transversum and is, therefore, attached along its entire surface; but later the area of its attachment becomes smaller, and the coelomic cavity partially surrounds it, even on its superior aspect. This uncovered inferior aspect of the diaphragm has its chief source in the muscle elements that begin to develop opposite the fifth cervical somite.

An understanding of the foregoing mechanism makes it easy to appreciate why congenital defects or weak areas in the diaphragm are usually in the posterior half of the diaphragm, for it is there that the fusion of its main contributing elements occurs (Fig. 1). Moreover, the fact that the liver at one time covers the whole inferior surface of the septum transversum would lead to the deduction that deficiencies in that portion of the diaphragm resulting from development of the septum transversum would be very rare; which, indeed, is the case. Moreover, since the pleuroperitoneal hiatus is the last portion of the pleuroperitoneal canal to close, it is easy to see how there is greatest tendency for hernias to occur at this point; and this is clinically the region where such defects are commonly located. The explanation of the other type of lesion commonly noticed, i. e., a herniation through the esophageal opening, arises from the fact that the stomach begins to differentiate as a bulging of the entodermic canal while still a thoracic organ,[22] and that if its descent is delayed it may present its greatest width at the level of the diaphragm just at the time when its various component parts are uniting, thus leaving a wider opening than is usual. Accord-

22. Bailey, P.: A Case of Thoracic Stomach, Anat. Rec. **17**:11, 107, 1919.

ing to Hume,[6] the types of congenital diaphragmatic hernia may be classified as arising as follows:

1. Through the hiatus pleuroperitonealis. This is the commonest type and is probably due to the gut's following the lung bud as it leaves the abdominal cavity (always false).

2. Through the dome of the diaphragm. This may be true or false and may be caused by a weak point in the diaphragm. These cases are often associated with incomplete rotation of the gut.

3. Through the esophageal orifice. The stomach may fail to migrate below the diaphragm or may migrate late, leaving a large esophageal opening.

4. The entire left half of the diaphragm may be absent. This is very rare, but has been found.

There are in addition a few unusual forms found. Eight cases have been reported of hernias through the foramen of Morgagni and two through the orifice for the sympathetic trunk.

From a review of the literature, it is clear that congenital deficiency of the diaphragm has been noticed much more frequently on the left side than on the right. Truesdale [23] places the proportion of left sided lesions to those of the right side at eight to one. The theory that the liver protects the right side of the diaphragm does not seem entirely adequate,[24] as the liver is formed under the septum transversum and during a large part of embryonic life protects the left side as much as the right. Is it not possible that the explanation lies in the distribution of the vascular elements which play such an important part in the early formation of the embryo? In support of this view, we wish to advance the following facts for consideration.

1. The position of the pulmonary ridge of Mall and the pleuroperitoneal membrane is determined by the common cardinal veins. The common cardinal vein on the right grows and forms the superior vena cava. The common cardinal on the left atrophies and its distal portion disappears in the 20 mm. human embryo. It seems that this would tend toward a weakness of the left pleuroperitoneal membrane.

2. In the 2.5 mm. embryo, the liver becomes adherent to the dorsal body wall on the right to allow the formation of the vein of the plica venae cavae, which becomes the inferior vena cava.

3. In the 3.5 mm. embryo, the tubal heart loops over to the right preparatory to the formation of the atria and ventricle.

4. In the 4.5 mm. embryo, the right half of the sinus venosus is observed to be growing much faster than the left.

---

23. Truesdale, P. E.: Diaphragmatic Hernia: the Thoracic Approach, Ann. Surg. **74**:347-354 (Sept.) 1921.

24. Beckman, E. H.: Diaphragmatic Hernia with Report of Three Cases, Surg., Gynec. & Obst. **9**:154-166, 1909.

It seems probable that the vascular concentration in the region of the right side of the diaphragm would contribute to the strengthening and blocking of the pleuroperitoneal canal, while the atrophy of the common cardinal vein on the left would contribute to the weakening of the left half of the diaphragm.

The foregoing considerations seem to show that there is a sensible embryologic explanation for these diaphragmatic lesions, and further they demonstrate the reasons for the known greater frequency of defects over true hernia. A study of the following case reveals a peculiar type of defect in that the opening is not only in the anterior portion of the diaphragm but is on the right side.

OBSERVATIONS FOLLOWING OPERATION, IN A DOG

A female Sealyham, 1 year old, in heat, was brought to the laboratory to be spayed. The owner, a physician, had acquired the dog when she was 8 weeks old and as the animal seemed healthy, no history was obtained from the former owner. After a discussion as to the benefits of hysterectomy over oophorectomy in such a case, provided the owner wished to preserve the dog's clean figure and eager disposition, it was decided to spay the animal.

Operation was performed at 2 p. m. No breakfast had been given. Morphin gm. 0.01 hypodermically was given and half an hour later ether anesthesia (cone method) was started. The abdomen was shaved, and under aseptic conditions opened in the midline for about 2 inches (5 cm.) midway from ensiform to pubes. Nothing abnormal was noted. The ovarian pedicles were tied off and both ovaries removed. Closure was performed in layers. The operation required twenty minutes; anesthesia was satisfactory throughout, and the dog seemed in good condition at the close of the operation.

During the next ten minutes of recovery, as the effects of ether wore off, the animal tried to vomit. It was then noticed that during these attemps, always unsuccessful, the general condition of the animal rapidly deteriorated. In fact, this became so obvious that a stetoscope was placed over the heart, when it was found that, with each attempt to vomit, the heart beats rapidly increased in rate and diminished in force. With increased efforts to vomit, the heart failed rapidly, and finally ceased. It was then remembered that following the administration of morphin an unsuccessful attempt to vomit had also been noticed.

Necropsy was performed immediately. It was then discovered that the fundus of the stomach, the spleen, part of the great omentum, about two thirds of the liver, and the gallbladder were in the right thoracic cavity, having migrated there through an opening in the anterior portion of the right diaphragm. There was a small amount of blood in the abdominal cavity (not enough to color one sponge). The ovarian ties were holding. Otherwise, the abdomen was negative. On further observation, it was found that the anterior and anterolateral portions of the right half of the diaphragm were indicated by a muscular band 1 cm. high projecting from the walls of the body cavity, thus leaving an oval deficiency with the following dimensions: anteroposterior, 4 cm.; lateral, 6 cm. This opening was situated in the muscular portion anterior to the tendon (Fig. 5). It was surrounded by a firm fibrous ring. The rest of the diaphragm was well developed and normal, except for a fold near the posterior rim of the opening, doubtless caused by the stretching of the ring by the viscera. The anteromedial border of the opening coincided with the attachment of the

pericardium to the superior aspect of the diaphragm. At this point, there was another opening 5 mm. in diameter communicating with the portion of the pleural cavity occupied by the intermediate lobe of the right lung. This opening was also surrounded by a firm fibrous ring. Immediately inferior to this hole and superior to the phrenic nerve was an opening 1 cm. in diameter, which was in the same partition and against which a projection of the liver rested.

The stomach was turned in such a way as to allow the fundus to protrude through the opening in the diaphragm into the anterior portion of the right thorax. It had carried with it part of the great omentum and the spleen. The

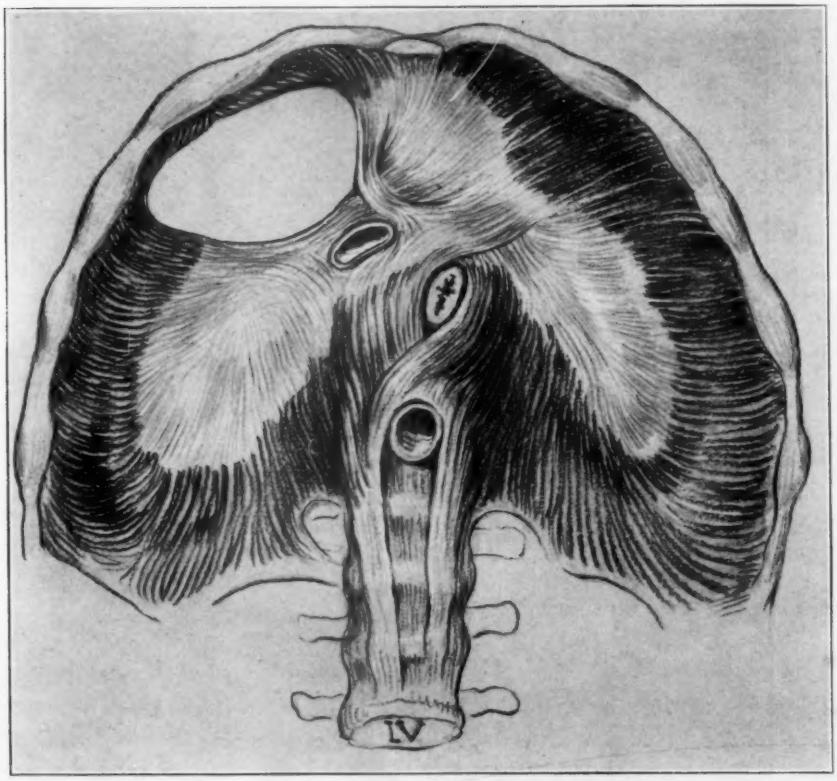

Fig. 5.—Diaphragm (after Gray) with defect reconstructed as to position and relative size.

left superior portion of the abdominal cavity, ordinarily occupied by the fundus of the stomach and spleen, was filled with coils of the small intestine.

The liver was located on the right side, its long axis corresponding to the long axis of the body cavity. It extended along the posterior body wall from the third thoracic to the third lumbar vertebra. The left lateral, left central and quadrate lobes, as well as the gallbladder, were in the right thorax, while the right lateral, caudate and papillary lobes were in the abdomen. The thoracic portion of the liver filled the posterior and postero-inferior portions of the thoracic cavity. It was rather distorted in shape, its free border being folded on itself in several places. The costal surface showed grooves to accommodate

the ribs. The anterior surface contained a distinct depression into which the fundus of the stomach fitted. There was a short ligament running from the inferior and medial angle of the left lateral lobe of the liver to the anteriomedial border of the opening in the diaphragm, at a point closely related to the small opening; into the space occupied by the intermediate lobe of the right lung

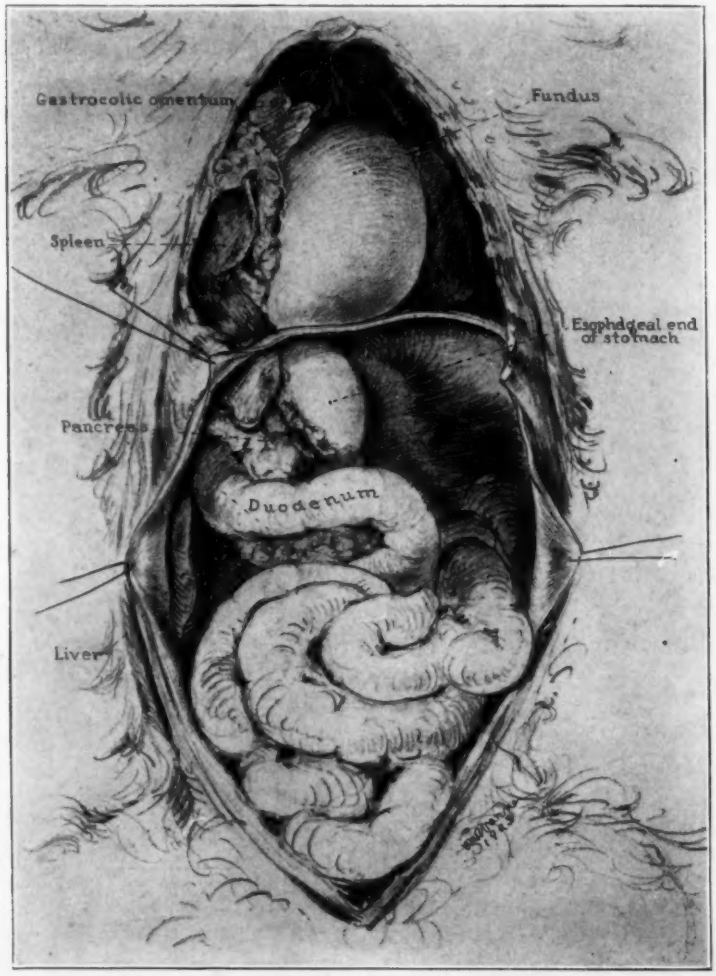

Fig. 6.—Appearance immediately after death; position of abdominal viscera in thorax. The narrowing and kinking of the cardiac end of the stomach where it lies in the diaphragmatic opening; the displacement of the heart and its relation to the distended stomach, and the position of the spleen may be noted. The portion of the liver in the thorax lies behind the spleen and stomach.

(described above). This was the only thoracic attachment of the liver, the main attachment being on the inferior surface of the diaphragm.

The cecum was situated in the right superior portion of the abdominal cavity. Otherwise, the intestines and mesenteries were normal.

The right kidney was somewhat larger than the left kidney. It was also somewhat lower, its upper pole corresponding to the second lumbar vertebra, while that of the left kidney corresponded to the first lumbar vertebra.

All organs not specifically mentioned were entirely normal. The drawings (Figs. 6 and 7) and photographs (Figs. 8 and 9) demonstrate the general condition.

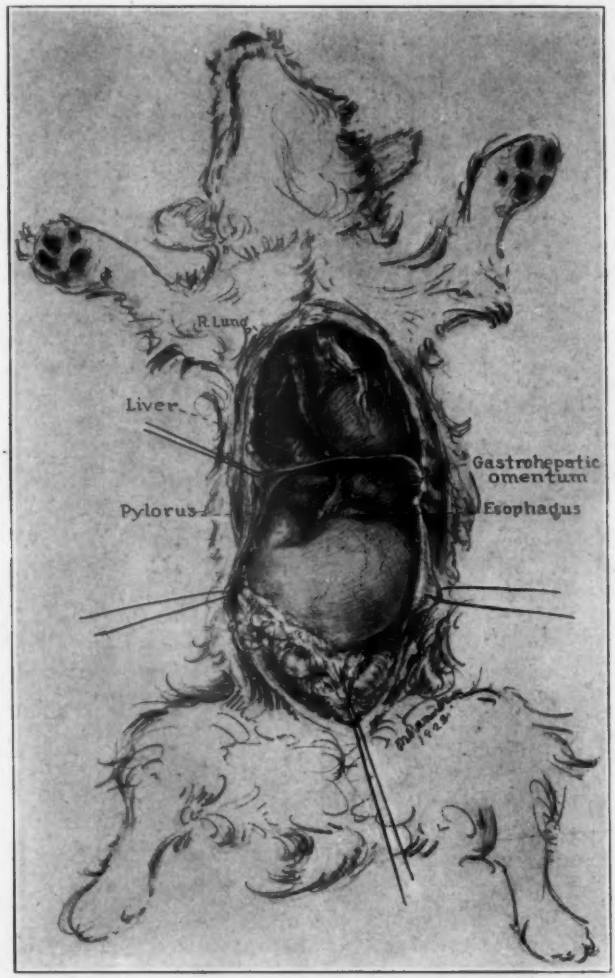

Fig. 7.—Appearance shortly after death, after the stomach and spleen had been pulled back into the abdominal cavity. The large amount of liver tissue visible in the thorax from this angle and the small ridge of diaphragm anteriorly may be noted. The latter diminished to almost nothing on the lateral wall.

The death of the animal may be explained thus: During anesthesia in the recumbent position, with added intra-abdominal pressure from wet gauze sponges and retraction, the stomach migrated into the thoracic cavity through the defect in the diaphragm. Since the stomach was found distended with air,

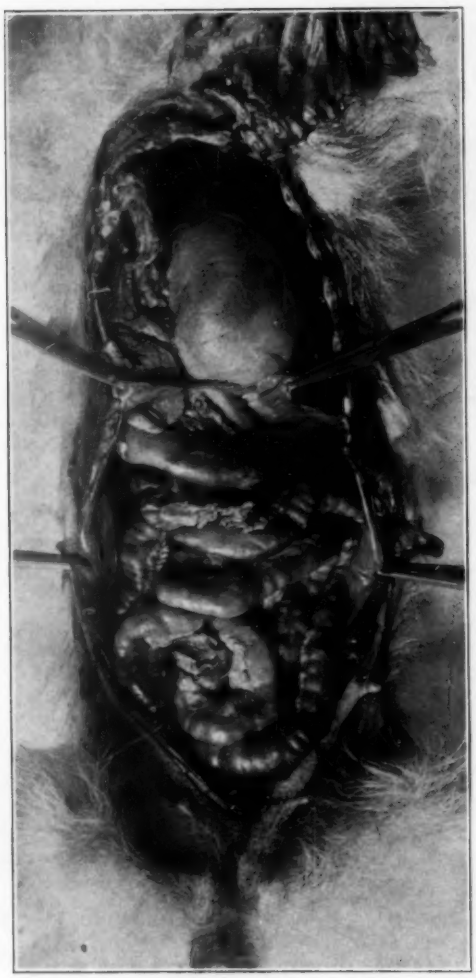

Figure 8

Figure 9

Fig. 8.—Appearance the day after death (preservation in cold chamber); showing actual position of viscera (compare legend of Figure 6).

Fig. 9.—Condition after replacement of stomach and spleen in abdominal cavity. The gastrohepatic omentum running through the opening in the diaphragm to the liver in the thorax may be noted. It was just on the thoracic side of the partition at the upper limits of the attachment of the gastrohepatic omentum that the second anomalous opening through into the subcardial space was found. The liver was also adherent at this spot, giving the impression that the opening may have occurred just at that portion of the diaphragm formed by the junction of the septum transversum and right pleuroperitoneal membranes.

some air must have been swallowed during the primary stage of anesthetization (as is known to occur), and more in the struggle during recovery. But the kink in the esophagus was such that air, once in, found difficulty in returning via the esophagus, as was seen from the dog's inability to vomit. Thus, with each attempt to vomit and because of the pressure exerted by abdominal muscles, there was a tendency for more of the intestine to be pushed into the thorax, and for a sudden increase in intrathoracic pressure. It is quite possible that during the operation some air leaked into the pleural cavities as in a thoracostomy, thereby increasing the difficulties of respiration. The foregoing factors must have diminished the animal's ability to oxygenate its blood sufficiently as well as have exerted considerable deleterious effects by direct pressure on the heart.

These findings having been determined, a history of previous difficulties was sought for, and a recital of symptoms similar in many respects to those present in human beings suffering from the same lesion was obtained from the family's chauffeur, without his knowing the foregoing findings. He had noticed that one day, about four months before death, the dog while running barking after a horse and wagon, suddenly became very short of breath and vomited profusely. For a period of two weeks thereafter, she vomited practically all solid food taken. From this time to the time of death, she was unable to exert herself without becoming short of breath and vomiting. On some of these subsequent attacks, she vomited all food taken for one or two days. It was further noticed that she occasionally went through "changes of shape." At such times, the abdomen would appear much distended or the lower part of the right thorax would enlarge.

COMMENT

This case would seem to come into the general division of congenital deficiency of the diaphragm. There was no history of severe trauma, and it seems that had an injury occurred sufficient to produce a large hole in the diaphragm, the general and local reactions to it would have been recognized by the family, in which this animal was a great pet.

It is true that congenital lesions in the right diaphragm are rare and that they are especially rare in the anterior portion. This lesion can be explained as a failure of normal developmental processes and the small defect, described above and located at the junction of the pericardium with the diaphragm, can be considered as bringing considerable weight in such a classification. This second defect certainly cannot be explained on any other basis, and is best explained by some failure in the development of the right pleuropericardial membrane at its point of juncture with the septum transversum. When we consider that the relationship between the pleuropericardial and pleuroperitoneal membranes is most intimate, and we find lesions in adult structures derived from these membranes, for one at least of which there seems none other than a congenital deformity as the explanation, it seems reasonable to conclude that both lesions are congenital in origin.

The mechanism of the causations of the early defect will always be obscure, but in the instance cited it may possibly be connected with an

anomalous involution of some of the vascular elements (inferior-superior cardinal veins) for the support of which these membranes exist. Thus, we have put the congenital defect in our case as occurring in the right pleuroperitoneal membrane, a structure which, as we have shown, plays a most important rôle in the development of the diaphragm. It is true that criticism of such an explanation may be made in that the defect in this instance was far forward, whereas that portion of the diaphragm derived from this membrane has usually been thought to be the posterolateral portion. In defense, we would say that a study of these embryologic structures and their development leads one to indulge in much latitude as to just what portions of the adult diaphragm are descended from the original sources of which it is composed. It seems that the septum transversum really fails to increase in size proportionately and actually forms what in the adult is limited to the portion immediately subcardial; whereas, the portion derived from the body wall constantly increases in relation to the whole diaphragm. The fact that, in our case, the liver and gastrohepatic omentum were adherent to the lower angle of this second opening led us to conclude that a portion even of this defect came from the septum transversum, since we know the liver develops in the ventral aspect of this structure. This is of much interest, and taken in conjunction with what appears as the very large liver, leads us to the explanation that, because of an early defect in the thoraco-abdominal partition, the liver pushed through into the thorax, bending into this cavity the edge of the septum transversum and impeding thereby both the progressive completion of the diaphragm through growth of those portions derived from the pleuroperitoneal membrane and body wall, as well as interfering with the final growth of the pleuropericardial membrane.

In some of the case reports, additional congenital defects have been found, especially defects of the lungs (Cockayne and Gladstone,[25] Rawes,[26]) or aberrant lung tissue, as well as congenital lesions of the heart. In our case, no such defects could be found, though carefully searched for.

A study of the literature reveals a large number of case reports,[27] with a general tendency to group the cases as either of acquired or of congenital origin. The number of false hernias or defects of the diaphragm greatly predominate over the cases of true hernia.[28] Such

25. Cockayne, E. A., and Gladstone, R. J.: J. Anat. **52**:64, 1917.

26. Rawes, L.: Congenital Diaphragmatic Hernia Associated with Embryonic Organs, Brit. M. J. **2**:884, 1911.

27. Scudder, C. L.: A Case of Nontraumatic Diaphragmatic Hernia, Surg., Gynec. & Obst. **15**:261-267, 1912.

28. Vogel, K. M.: Diaphragmatic Hernia, with Report of a Case, Am. J. M. Sc. **145**:206-209, 1913.

lesions have been found most frequently at the esophageal opening, with openings in the left posterior portion of the diaphragm next in frequency. A few cases of complete absence of the left half of the diaphragm are on record (Gross,[29] Livingston,[30] Monks,[31]). Right sided lesions (Beckman,[24] Kakels and Basch,[32] Keith,[33] Shafer [34]) are extremely rare, and only now and then are cases reported in which the herniation occurs at the openings for the hypogastric arteries (anteriorly) or for the sympathetic trunks (posteriorly). The number of proven acquired cases, except those due to direct perforation by a missile of war (Andrew,[35] Keenan [36]), are few, and in these usually the left side was involved (Hume,[6] Keenan [36]). The embryologic etiology for the congenital type has been fully discussed, and the reported cases fulfil by their location what could be predicted from a knowledge of the growth and development of the diaphragm. All of the abdominal organs, with the exception of the rectum, bladder and genitalia, have been found within the thorax in such cases (Bell,[7] Martland,[37] Scudder [38]).

There are no pathognomonic signs and symptoms of such lesions, for the picture presented varies individually with the extent of the opening, and more particularly with the herniated viscera. It is unnecessary to discuss the diagnosis of the acute acquired traumatic case further than to say that, in any missile wound of the abdomen or thorax, one should attempt to map out the trajectory and subsequent

---

29. Gross, L.: Hernia Diaphragmatica Vera (Congenital Absence of the Left Side of the Diaphragm, Dextrocardia; Tubular Stenosis of the Aorta; Malformation of the Liver and Lungs), J. Med. Res. **38**:473-475 (July) 1918.

30. Livingston, P.: A Case of Congenital Diaphragmatic Hernia, Am. J. Obst. **15**:733-738, 1882.

31. Monks, E. H.: Deficiency of the Left Half of the Diaphragm, with Displacement of the Stomach and Other Abdominal Organs, Brit. M. J. **1**:708, 1914.

32. Kakels, M. S., and Basch, S.: Diaphragmatic Hernia Into the Right Thoracic Cavity, Med. Rec. **86**:655, 1914.

33. Keith, D. Y.: A True Congenital Hernia in the Right Diaphragm, Am. J. Roentgenol. **7**:289-291 (June) 1920.

34. Shafer, L. C.: Congenital False Right Diaphragmatic Hernia, Tr. Chicago Path. Soc. **10**:222-226, 1917-1918.

35. Andrew, J. G.: Diaphragmatic Hernia of Entire Stomach and Great Omentum, Brit. Med. Jour., **2**:412 (Sept. 27) 1919.

36. Keenan, C. B.: Traumatic Diaphragmatic Hernia, Ann. Surg. **75**:625-626 (May) 1922.

37. Martland, H. S.: A Case of Congenital False Diaphragmatic Hernia, Proc. New York Path. Soc. **8**:189-191, N. S., 1909.

38. Scudder, C. L.: A Case of Nontraumatic Diaphragmatic Hernia; Operation; Recovery, Tr. Am. Surg. Ass'n **30**:428-447, 1912.

course of the missile after entrance, and should always consider the possibility of the penetration of such a missile into the neighboring body cavity.

The symptoms which may appear in children with such a lesion are usually due to herniation through a relatively large opening of a considerable portion of the abdominal gastro-intestinal tract. This may occur as the result of straining or changing position and may result in an acute dyspnea, with asphyxia. Physical examination should reveal unusual tympanitis over parts of the chest wall on percussion, and borborygmi and distant or obscure breath sounds on auscultation. In the adult or the child, herniation through a small opening may result in kinking of the intestine, and all the signs and symptoms of intestinal obstruction. Also cases are reported of the rupture of a peptic ulcer or of the occurrence of acute appendicitis in these respective organs when present in the thoracic cavity. If in the examination of a patient suspected of empyema, fetid air rushes out through the exploring needle, the possibility of one of the foregoing conditions must be considered. But in the majority of cases, there occur either no symptoms or at best vague sensations qualified as indigestion. These sensations seem often similar to those experienced in patients with gallbladder disease in the interval between acute attacks characterized as heartburn, biliousness, gaseous eructations, etc., and sometimes these symptoms are brought into prominence by a change of position or by straining or lifting (DeCourcy,[39] Soresi [40]). Giffin [2] speaks of three primary symptoms: (1) epigastric pain, (2) paroxysms of smothering and (3) vomiting. The roentgen ray must confirm any suspicion of this trouble and is, indeed, our chief reliance (Frank,[5] Grandy,[41] Scudder [42]). Care should be taken that the examination following an opaque meal is made with the patient both lying and standing, and with pressure on the abdomen. Special emphasis should be placed on following out the limits and action of the diaphragm and on any displacement of the heart. Roentgenograms should always be taken for further corroboration and study after fluoroscopy.

The condition of eventration may closely simulate in its signs and symptoms true and false hernia,[16] but a careful roentgen-ray study should permit differentiation.

Treatment must be surgical, though it is obvious that a sedentary life will tend to keep acute trouble in the background. In adults, except for the acute and obstructive aspects of this condition, the symptoms are

---

39. DeCourcy, J. L.: Diaphragmatic Hernia, Ann. Surg. **70**:179 (Aug.) 1919.

40. Soresi, A. L.: Diaphragmatic Hernia, Ann. Surg. **69**:254 (March) 1919.

41. Grandy, C. C.: A Case of Diaphragmatic Hernia Diagnosed by Roentgen Ray, J. A. M. A. **64**:1237 (April 10) 1915.

42. Scudder, C. L.: Diaphragmatic Hernia, Ann. Surg. **56**:348, 1912.

usually insignificant and the finding of the condition is incidental [43] to a complete roentgen-ray study of the gastro-intestinal tract. In such cases, surgery would be meddlesome.

If surgery seems necessary, the thoracic route seems to be the one of choice, and the opposition to this method by men accustomed chiefly to abdominal surgery on the grounds that it creates a dangerous artificial pneumothorax is indefensible if only because the same condition must also occur in the much more difficult approach through the abdomen (Barton,[44] Beckman,[24] Downes,[45] Scudder [37]). By excision of the sixth, seventh or eighth ribs posteriorly and laterally, an excellent and simple exposure of the diaphragm is obtained.

---

43. Within six months at the Peter Bent Brigham Hospital, two cases of this condition were encountered, in both of which the hernia was at the esophageal opening. The first patient came in because of gallbladder trouble, and at operation a gallbladder full of stones was removed. The second patient was in the hospital for an operation for piles.

44. Barton, J. A. B. D.: A Case of Diaphragmatic Hernia, Brit. Med. Jour. **1**:767 (June 21) 1919.

45. Downes, W. A.: Congenital Hernia of the Diaphragm, Surg., Gynec. & Obst. **27**:393 (Oct.) 1918; Tr. Am. Surg. Ass'n **36**:410-420, 453, 1918.

FURTHER OBSERVATIONS ON PEARLY TUMORS*

PERCIVAL BAILEY, M.D., PH.D.
Junior Associate in Surgery, Peter Bent Brigham Hospital
BOSTON

In 1920, I had occasion to describe two rather rare tumors of the type first depicted by Cruveilhier [1] under the name "tumeurs perlées." Since then, the observations which follow, as well as the articles of Cushing [2] and Horrax,[3] have cleared up many doubtful points in my original description.

The cases reported in 1920, the ones detailed by Cushing and Horrax, and those which follow, all belong to the class known to Bostroem [4] as *piale Epidermoide*. They have also been termed "tumeurs perlées" and "cholesteatomas." None of these terms is satisfactory, for various reasons. There are, for example, the pearly tumors so often found in the lateral ventricle of the horse, which have nothing in common with the growths under discussion except the glistening pearly surface. The term cholesteatomas is no less objectionable because often cholesterin is not present, and furthermore, tumors of the breast, testicle, etc., of entirely different nature may contain cholesterin. The term *piale Epidermoide* is hardly more appropriate since these tumors may be extradural and so have no connection whatever with the pia mater. It still seems to me that the best designation is pearly tumor. The only other neoplasms with which they might be confused under this name are the ones found in the lateral ventricles, particularly of the horse, which are structurally entirely different.

Whatever the terminology employed, the growths are quite unmistakable: masses of epithelial cells of characteristic structure, which may or may not contain hair, or cholesterin crystals, and whose surface has usually the appearance of mother-of-pearl. Histologically, they are composed of a fine fibrous wall whose inner surface is covered by layers of flattened cells containing keratohyalin granules, and also of masses of cells flattened and structureless, or with only the

---

* From the Surgical Clinic of Dr. Harvey Cushing.
* Read at the Peter Bent Brigham Hospital Reunion, May 24, 1923.

1. Cruveilhier: Anat. path. du corps humaine **1**, Book 2, Plate 6, 1829.
2. Cushing, Harvey: Surg., Gynec. & Obst. **34**:557 (May) 1922.
3. Horrax, Gilbert: Dermal Versus Epidermal Cholesteatomas Having Their Attachments in Cerebral Envelopes, Arch. Neurol. & Psychiat. **8**:265 (Sept.) 1922.
4. Bostroem: Centralbl. f. allg. Path. u. path. Anat. **8**:2, 1897.

intercellular substance remaining, giving the appearance of the cells of woody plants. The interior may be a broken down mass of débris containing fatty material and cholesterin crystals.

The favorite location for these collections of epithelial cells is in the pia mater around the base of the brain. They may project upward into the cerebellopontile angle, the fissure of Sylvius, between the frontal lobes or into the third ventricle. They often occur extradurally under the parietal or temporal bones. Rarely, they may be found in the fourth ventricle, and more frequently in the middle-ear cavity.

PEARLY TUMORS OF THE MIDDLE EAR

The development of primary tumors of this type in the middle ear was long disputed. That they do occur was finally established by Erdheim.[5] He, in 1905, described a specimen removed from a 36-year-old woman who had never suffered from otitis media. The middle-ear cavity was intact and entirely normal. Nowhere was there any thickening of the lining or the slightest suspicion of suppuration. The structure of the growth was quite characteristic. Underneath the connective tissue capsule was a layer of stratified epithelium from two to eight cells in thickness. These cells contained keratohyalin granules and were united by delicate intercellular bridges. The interior was made up of masses of flattened cornified cells.

Similar instances had been published by Lucae,[6] Schwartze[7] and Körner,[8] but the presence of a coexisting inflammation or an old perforation of the drum membrane had prevented them from being conclusive, in view of the work of Habermann.[9] It was the belief of Habermann, and of many others, that these masses of epithelial cells were the result of proliferation of the cells lining the cavity of the middle ear, under the influence of chronic suppuration and perforation of the tympanic membrane.

There is abundant evidence to show that the normal epithelial lining of the middlle-ear cavity is always replaced by squamous epithelium after long-standing perforation of the drum. But, although the caseous residue of an old suppuration may contain cholesterin and may closely resemble the material from the interior of a pearly tumor, when it is removed, it will be found, microscopically, to be free from the peculiar woody-plant-like cells and from all trace of an epithelial sac.

---

5. Erdheim: Ztschr. f. Ohrenh. **49**:281, 1905.
6. Lucae: Arch. f. Ohrenh., n. f. **1**:255, 1873.
7. Schwartze: Arch. f. Ohrenh. **41**:207, 1896.
8. Körner: Ztschr. f. Ohrenh. **37**:352, 1902.
9. Habermann: Ztschr. f. Heilk. **21**:, 1900, chir. abt., p. 173.

Wingrave [10] says of the structure of the granulomatous variety of cholesteatoma of the middle ear that it is very different from the primary tumors. "Granulomatous elements covered with stratified epithelium will be found embedded in loose lymphocytes, leukocytes, myeloblasts, and squames in all stages of fatty and granular change. The squames may be loose or grouped in closely laminated 'pearls' having for the most part lost their nuclei and become strongly acid-fast. Bacteria of all kinds are mixed with the cells and the throat organisms —spirochetes, fusiform bacilli, yeasts, leptothrices, cladothrices, etc."

The course of events in the case of primary growth was well outlined by Körner. The tumor lies for a long while dormant, or giving only negligible symptoms, but its presence predisposes the ear to infection, for which the patient first comes to the clinic. By that time, the tumor mass may have been involved in the inflammatory process and its original structure may be much altered. It is then believed to have been secondary to the old suppuration.

In Case 1, which recently occurred in this clinic, there was an old infection of the middle ear, but the tumor mass was not involved.

CASE 1.—*Pearly tumor of the middle ear cavity; extirpation; recovery. History.*—C. B., aged 62, a laborer, referred by Dr. L. W. Dean, Utica, N. Y., and admitted Nov. 15, 1922, complained of dizziness and a sense of pressure in the head.

The family history was negative. In 1892, the patient had an operation on the left ear for polypi and a discharge. The discharge ceased shortly and, except for a period of two months in 1902, had not returned. During the autumn of 1920, the patient began to have attacks of vertigo and a sense of pressure in the frontal region. The attacks lasted ten or fifteen minutes, and during them he noticed a tendency to fall to the right. At the onset, he complained of a noise in the left ear like the puffing of a locomotive. This had since disappeared. There has been no discharge from the ear during this time. A mastoid operation was performed in October, 1920, and a "cholesteatomatous" mass removed. Since the operation, the patient had been totally deaf in the left ear and had a left facial paralysis. The feeling of discomfort in the head continued to increase.

Physical Examination.—On admission, no evidence of intracranial disease was found. There was total deafness in the left ear and a left peripheral facial palsy. The pearly glistening surface of a tumor was visible in the depths of the left external auditory meatus.

Operation (November 28, by Dr. Cushing).—An incision was made concentric with that of the previous mastoid exploration and the ear was turned forward. With a burr, the mastoid was very largely cleared away, exposing the sinus and the lower part of the temporal dura. The bone was then removed upward and forward until the glistening wall of what proved to be a small pearly tumor was disclosed. The tumor, which measured about 2 cm. in diameter, was shelled out in its entirety, leaving a clean-walled cavity.

---

10. Wingrave: Proc. Roy. Soc. Med., London, Otol. Sect. **3**: 63-70, 1909-10.

Postoperative Course.—There was some bloody discharge from the ear for a few days. The patient was discharged, December 10, and reported, Jan. 3, 1923, that he was perfectly well, except that the sense of pressure in his head persisted.

Pathologic Examination.—The tumor removed consisted of a rounded mass of grayish white cheesy material surrounded by a pliable capsule with a lustrous mother-of-pearl sheen. The interior was quite friable and fell out of the microscopic preparations. Cross sections of the capsule were obtained (Fig. 1).

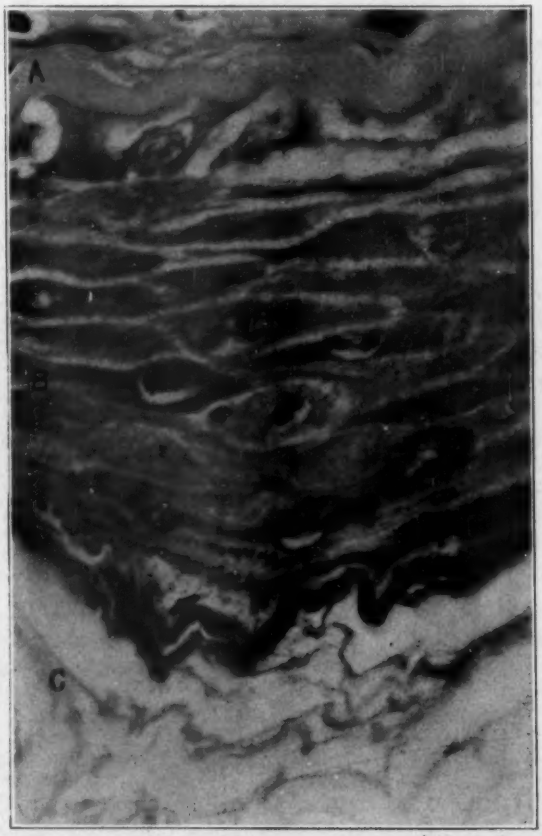

Fig. 1 (Case 1).—Cross section of capsule of pearly tumor of middle-ear cavity: *A*, stratum durum; *B*, stratum granulosum; *C*, stratum fibrosum. Intercellular bridges are seen between the cells of the stratum granulosum and keratohyalin granules in the lower layer; × 850.

On the outer surface was a layer composed of thick bundles of fibers staining heavily with anilin blue and with acid fuchsin. Then came a layer of stratified epithelium from six to twelve cells in thickness. The outer cells near the connective tissue were roughly quadrangular; the others were more and more flattened as the interior was approached. Delicate intercellular

bridges were clearly seen. The innermost cells contained numerous keratohyalin granules. The interior of the tumor was composed of flattened cornified lamellae. No "woody-plant" cells were seen and also no cholesterin crystals.

Both cholesterin and "woody-plant" cells were found in the interior in another typical case which I had an opportunity to examine through the kindness of Dr. Jeannette Shefferd of Fall River, Mass. The clinical history has already been published.[11] A cross section of the wall of this tumor is shown in Figure 2.

In neither of these pearly tumors from the middle ear was any evidence of inflammatory reaction found. Both were identical in structure with cases published in 1920,[12] from the third and fourth ventricles.

Fig. 2.—Cross section of capsule of a pearly tumor removed from the middle-ear cavity of M.S. (patient of Dr. Jeannette Sheffield): *B*, stratum granulosum; *C*, stratum fibrosum. The stratum durum is missing. Keratohyalin granules are faintly seen in the lower cells of stratum granulosum; × 850.

INTRADURAL PEARLY TUMORS

The most frequent location of these neoplasms is in the pia mater around the base of the brain, in a situation which would make surgical removal impossible except when the tumor material is of exceedingly friable consistency, as in the following case.

CASE 2.—*Pearly tumor of base of cranial cavity projecting into the third ventricle; extirpation; recovery. History.*—B. A., aged 40, formerly a salesman, referred by Dr. J. B. Green, Asheville, N. C., and admitted, Nov. 14, 1922, complained of loss of eyesight. The family history was negative. In 1914, the patient had a severe hemorrhage from the lungs. Diagnosis of pulmonary

11. Shefferd, J. M.: Boston M. & S. J. **186**:877 (June 29) 1922.
12. Bailey, Percival: Surg., Gynec. & Obst. **31**:390 (Oct.) 1920.

tuberculosis was confirmed by the roentgen-ray. Tuberculin therapy and outdoor living apparently brought about a cure. In 1917, the patient had a painful affection of the right foot, which was diagnosed tuberculosis. He wore a cast for a year, and since then had had no similar trouble.

The present illness developed in 1917, with severe headache. An oculist was consulted, and it was found that the acuity of vision in the left eye was much reduced. In 1919, vision failed to such an extent that the patient was obliged

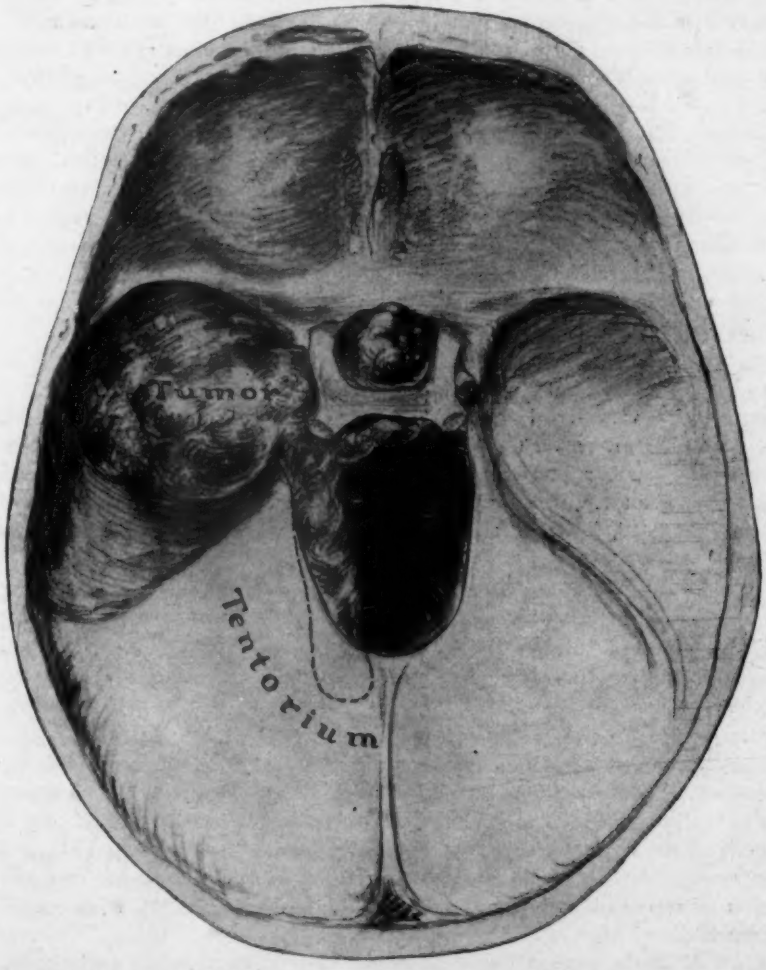

Fig. 3 (Case 2).—Drawing to show presumptive size and location of tumor.

to quit work, and he had since done nothing. He had been very irritable. In the last year, he had become weak, and libido sexualis completely disappeared.

He had had a long series of osteopathic treatments. At another clinic, an exploration of the region of the chiasm was advised, but the family refused to permit it.

Physical Examination.—There was a bilateral primary optic atrophy. With the right eye, he could see large objects in the left lower quadrant only. There

was nothing else definite in the way of neurologic findings. The basal metabolism was —13. The sella turcica appeared normal in the roentgenograms. Moist râles and prolonged expiration were heard over the right apex and the roentgen ray revealed an old tuberculous process in the apexes of both lungs. He seemed a little bizarre mentally, but no definite mental symptoms were recorded.

Operation (November 27, by Dr. Cushing).—A transfrontal exploration was undertaken on the left side because the left optic nerve was mostly affected. After elevation of the frontal lobe and incision of the dura, the left optic nerve was brought into view and then the right. Between them, the rounded, glistening mass of a pearly tumor was seen, about 1 cm. in diameter. This portion was scooped out with a pituitary spoon. It was then evident that there must be a tumor to the left of the optic nerve, and, on invesigation, a mass the size of a golf ball was exposed in the middle fossa. This was in turn scooped out and the fragments were washed and removed by suction. It was then seen that the growth extended beyond the tentorium, and it was pursued, in the same way, at least 2 inches (5 cm.) beyond the incisura, until the suction apparatus failed to bring away any more fragments dislodged by gentle scraping with the pituitary spoon. What must have been the extent of the tumor is shown by the sketch in Figure 3.

There had been no bleeding during removal, so the huge cavity was filled with salt solution and the wound carefully closed.

Postoperative Course.—There was a cerebrospinal fluid leak for a few days through the frontal sinus, which had been opened during the operation. The patient became very irrational and developed the clinical picture of a meningitis, with high afternoon temperature, rigid neck and Kernig and Brudzinski phenomena. Lumbar punctures improved the condition somewhat. Cultures of the spinal fluid were always negative. Since the bone flap was being gradually elevated, it was decided to reopen the wound to determine the local condition.

Second Operation (December 22).—Under procain anesthesia, the bone flap was reelevated. By puncture of the lateral ventricle, 30 c.c. of sterile, clear fluid was obtained. From the region of the tumor, more clear fluid was obtained, so it was considered unnecessary to explore further, and the wound was closed.

Postoperative Course.—The patient improved gradually, but at discharge still occasionally had an afternoon temperature of over 100 F. Vision in the right eye was about as before the first operation; in the left eye, it was completely lost. He was walking unaided around the ward, but somewhat unsteadily. He had a paresis of the left external rectus muscle, absence of the palatal reflexes, fine action tremor of both hands, general diminution of muscular power and exaggeration of the tendon reflexes in both lower extremities. He was mentally very much disoriented.

Jan. 8, 1923, the patient was discharged. For some time, he suffered from dizzy spells and headaches. When last seen, March 10, he was in excellent physical condition but his mental state was certainly less good than before operation. Vision had remained stationary.

Pathologic Examination.—The material removed at operation consisted of about 30 gm. of cheesy, friable, grayish white material. Scattered through it were fragments of the capsule—pliable sheets of glistening mother-of-pearl, of about the consistency of tinfoil.

A section through the capsule is shown in Figure 4. It consisted of a layer of from four to eight rows of flattened epithelial cells, the innermost of which contained keratohyalin granules. The interior of the mass was made up of lamellae of cornified material, for the most part structureless. However, certain areas showed the characteristic box-shaped cells resembling those of woody plants.

Nowhere could any connective-tissue coat be found on the outside. Cholesterin crystals were found in the interior.

In 1920, but eight previous observations could be found of pearly tumors in the fourth ventricle. The following case is interesting as an almost exact duplicate of the case K. S., which I reported at that time.[11]

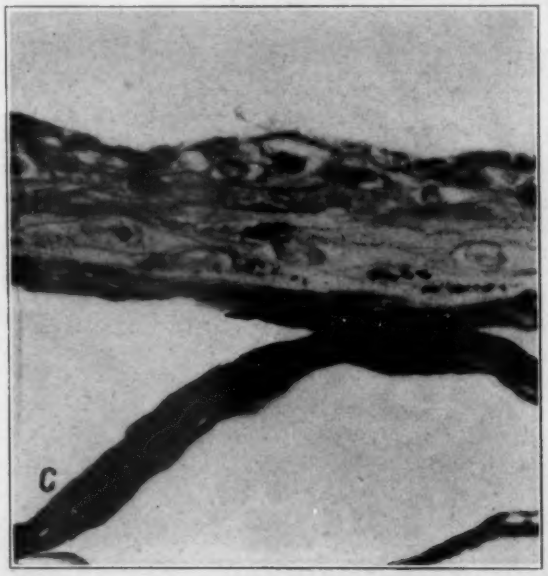

Fig. 4 (Case 2).—Cross section of capsule of tumor: *B*, stratum granulosum, showing keratohyalin granules in lowermost cells; *C*, stratum fibrosum. The stratum durum is absent; × 850.

Case 3.—*Pearly tumor of fourth ventricle; extirpation; recovery. History.*—J. M., aged 39, a groom, referred by Dr. Edwin A. Locke of Boston and admitted, Dec. 16, 1921, complained of pain in the back of the head, dizzy spells, unsteadiness of gait, double vision and vomiting. The family history was negative, and the personal history irrelevant. In the autumn of 1920, the patient began to have pain in the back of the head, the attacks being followed by periods of complete freedom from pain. The headaches became gradually generalized and in the last six weeks had been very severe.

In May, 1921, he began slowly to lose his eyesight. In July, for the first time, he vomited during a severe headache, and this vomiting had recurred half a dozen times since. He began also to have attacks of dizziness and twice fell

in the street. About the same time, he noticed that he walked unsteadily, as though he were drunk. He had noticed transient double vision since October.

Physical Examination.—Subocçipital tenderness on the right side, bilateral choked disk with elevation of 4 diopters, development of coarse nystagmus on looking to the right and left, unsteadiness of station and gait, and slight incoordination of all the extremities of cerebellar type, more marked on the left side, were revealed.

Operation (December 20, by Dr. Cushing).—The usual crossbow approach was made without difficulty. The left lateral ventricle was punctured and a great amount of fluid obtained. When the dura was opened, the hemispheres appeared normal, and exploration of the recesses disclosed no tumor; but when the two hemispheres, which had herniated down into the foramen, were separated, the glistening surface of a pearly tumor was seen. The vermis was split and held apart, and a good view of the tumor was obtained. It was found impossible

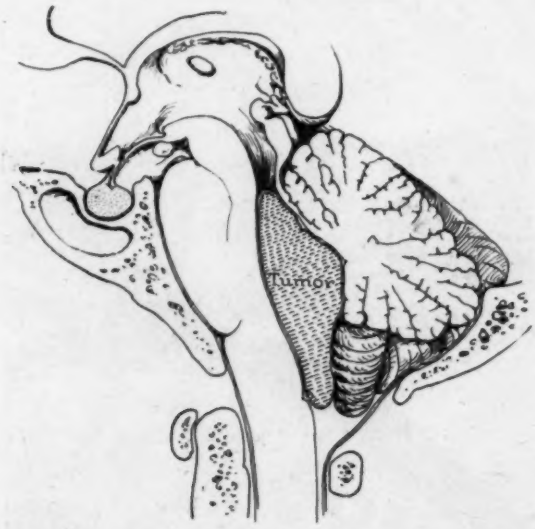

Fig. 5 (Case 3).—Presumptive size and location of pearly tumor.

to remove the capsule as had been done in the case of K. S.,[1] because some large vessels were firmly attached to it. However, as the tumor was soft, the contents were scooped out with a pituitary spoon. About 15 gm. of material was removed, consisting of a friable, cheesy grayish white mass. A few cholesterin crystals were seen in the cerebrospinal fluid. After removal of the tumor, one could look well up into the iter, as in the case of K. S. The area was thoroughly irrigated with physiologic sodium chlorid solution to remove fragments, and the wound was closed as usual. The approximate size and position of the growth is shown in the diagram of Figure 5.

Postoperative Course.—There was a transitory hyperthermia, reaching 104 F., after which recovery was uninterrupted except for annoying and persistent hiccup.

Jan. 19, 1922, the patient was discharged. The choked disks had given place to a secondary atrophy, and pressure symptoms were entirely relieved. The patient's gait was still rather unsteady and the nystagmus persisted.

Fig. 6 (Case 3).—Cross section of wall of tumor: *B*, stratum granulosum; *C*, stratum fibrosum. The stratum durum is absent; × 850.

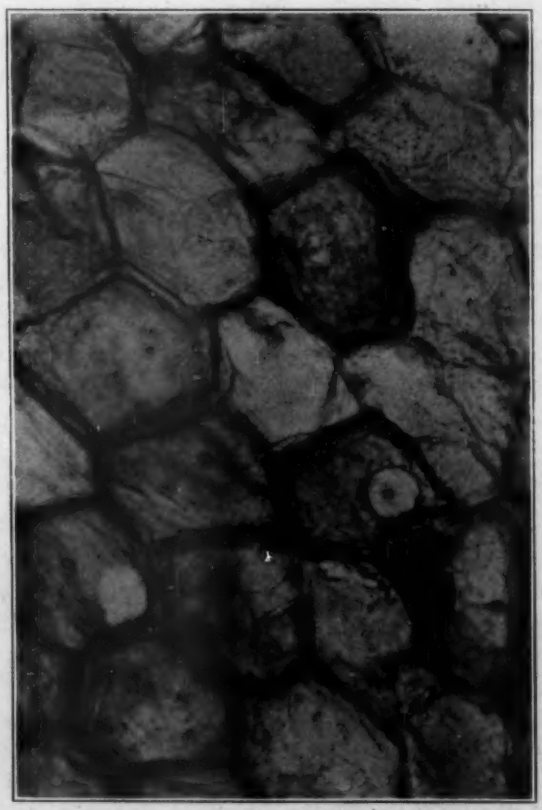

Fig. 7 (Case 3).—Cells of the stratum cellulosum. Similar cells were found in the interior of the other tumors reported; × 850.

Pathologic Examination.—The material removed consisted of about 15 gm. of a cheesy grayish white substance. Some fragments of the capsule were obtained.

A cross section of the capsule is shown in Figure 6. The epithelial layer was from three to eight cells in thickness. The cells were not so flattened as in the preceding cases and keratohyalin granules were not found. The interior of the tumor consisted of the boxlike cells resembling those of woody plants (Fig. 7). Even the cornified lamellae retained traces of cellular structure. At intervals, over the exterior of the epithelial cells, a delicate connective tissue covering was present. Many cholesterin crystals were found.

COMMENT

There can be no doubt that the tumors which have just been described all belong to the same class. They are definitely epithelial in origin. It would seem that no better example could be found of a tumor originating in a group of epithelial cells separated from its normal surroundings and developing autonomously.

Neoplasms of this type, as the preceding observations show (in accord with those of Bostroem, Erdheim, Cushing, Horrax and others), may occur intradurally, extradurally, or in the middle-ear cavity. Those occurring in the middle-ear cavity are primary growths and not secondary to suppurative or desquamative processes. It will be noted that in none of the tumors of the present report was hair found. That it may be present is definitely established by Horrax's Case III.[7] The capsule of the tumor in his case was in all respects identical with the capsule of the tumors described in the present report.

If we revert to the terminology employed in 1920, we may thus describe their histologic structure: The outer layer, or *stratum durum,* consists of connective-tissue cells and the collagenous fibers formed by them. It varies in thickness and may in some cases be absent. The second layer, or *stratum granulosum,* consists of epithelial cells, the deeper ones often containing numerous keratohyalin granules. Intercellular bridges are sometimes found between these cells. Beneath the stratum granulosum lies the *stratum fibrosum*[13] composed of flattened out and cornified cells, in which all evidence of cell structure may be lost. The *stratum cellulosum,* which makes up the bulk of the growth, is composed of cells which resemble very much those of woody plants. Often, only the intercellular substance is visible. In the interior of the tumor may be found cholesterin crystals and fatty material, and sometimes hair.

---

13. There is an error in my original description, in Surgery, Gynecology and Obstetrics, October, 1920. On page 12, line 34, one should read stratum fibrosum instead of stratum durum.

THE IMPORTANCE OF THE PERIOSTEUM AND THE ENDOSTEUM IN THE REPAIR OF TRANSPLANTED BONE*

S. L. HAAS, M.D.

SAN FRANCISCO

Almost two hundred years have elapsed since the beginning of the debate over the importance of the periosteum in bone growth, regeneration and repair; and in spite of the vast amount of experimental and clinical evidence submitted by the adherents of the two views, namely, the one that the periosteum is an osteogenic membrane, and the other that it is merely an inert limiting membrane, there exists today the same two factions, as in the early part of the eighteenth century.

In a most interesting review of this subject, Keith [1] presents many important facts connected with the early study of bone growth. He shows how Belchier,[2] in 1736, after investigating the chance observation of a calico printer who had found that the bones of his madder-fed pigs were stained red, discovered that only new bone took the red stain.

Duhamel,[3] in 1739, utilizing the important discovery of Belchier, came to the conclusion, from experimental work, that the new bone was formed by the periosteum, assisted by the endosteum.

No sooner had Duhamel's doctrine that the periosteum was osteogenic been announced than a faction arose under the leadership of Haller,[4] who maintained that the periosteum was not osteogenic. Haller maintained that the periosteum was merely a vascular covering that served for the nourishment of the bone, and that it took no part in the formation of repairing callus, or in the growth of bone. He believed that the callus was formed by the broken bones; that the arteries were the depositors and builders of bone, and that they could form bone anywhere within the limits of the periosteum.

The next important observer was John Hunter,[5] who began his epoch-making work about 1750. He was a firm believer in the teach-

---

*From the Surgical Laboratory of Stanford University School of Medicine.

1. Keith, Arthur: Bone Growth and Bone Repair, Brit. J. Surg. **5**:685 (April) 1918; **6**:19-24 (July) 1918; **6**:160-166 (Oct.) 1918.

2. Belchier, John: Tr. Phil. Soc. London **39**:287; quoted from Keith (Footnote 1).

3. Duhamel, H. L.: Sur une racine qui tent les os en rouge, 1739; quoted from Keith (Footnote 1).

4. Haller: Quoted from Keith (Footnote 1).

5. Hunter, John: Collected Works, **1** and **4**, London, James F. Palmer, 1837.

ings of Haller and did a considerable amount of investigating to confirm his opinions. He made the additional and important discovery that living tissue had the power to absorb bone. He upheld the belief that the arteries were the depositors of bone and that, in fractures, the deposition of bone usually commenced at the broken ends of the bone.

The death of Hunter occurred in 1793. Early in the nineteenth century the noted surgeon, James Syme, carried on his experimental investigations on the repair of bone. In 1835, he removed one and three quarter inches from the radius of both the right and the left legs of young dogs. On the right, he removed the periosteum, and on the left, this membrane was preserved in place. When the dog was killed at the end of six weeks, the missing portion of the left radius was regenerated; whereas, on the right, where the periosteum had not been preserved, a gap still remained. In another experiment, he placed tin-foil beneath the periosteum and found that the periosteum produced a layer of bone on the tin-foil. In still another experiment, he cut away the periosteum and wrapped tin-foil about the denuded bone, and he found that no new bone was formed on the tin-foil. Thus, the pendulum swings once again in favor of the osteogenic power of the periosteum.

With the advent of the microscope, it became possible to study the minute histologic structure of the various constitutents of bone, and to trace the different stages in its growth and development. John Goodsir,[6] working about 1841, had the opportunity of utilizing an improved microscope for the study of his specimens on bone growth. In spite of the fact that he worked with Syme, he came to diametrically opposite views regarding the function of the periosteum, concluding that it was not osteogenetic, but that in its removal small pieces of bone were carried with it and these grafts served as centers of reproduction for new bone. Although he was a follower of John Hunter, he found that it was not the arteries that formed the bone but specialized cells, the bone corpuscles, which also had the power to carry away bone. He conceived that, under the stimulation of inflammation, the canalicular cells became active, and further, from his study on the necrosis of shafts of long bones, he concluded that the periosteum had no bone forming power but was simply, as he termed it, "a limiting membrane," and that the regeneration which took place depended wholly on the proper substance of the shaft that became adherent to it. It is interesting to note how closely the ideas of the present day proponents of the nonosteogenic power of the periosteum correspond with those advocated by John Goodsir.

---

6. Turner, William: Anatomical Memoirs of John Goodsir **2**, 1868.

Contemporaneous with Goodsir was Marie Jean-Pierre Flourens,[7] who repeated Duhamel's experiments. In his works, published in 1842, he concluded that Duhamel was right, and that new bone was deposited on the surface of old bone, under and by the periosteum. He also agreed with Hunter that, coincident with bone building, there was bone absorption.

In the next period, we find the work of Ollier,[8] published in 1867, in which he touches on practically all the phases of bone growth and repair. He performed various experiments, to find out whether the periosteum was osteogenic. He turned out flaps of periosteum from the bone, about the neighboring muscles, and found that new bone was formed on the under surface of the periosteum. He found that periosteum transplanted to subcutaneous tissue formed bone. The opponents of the osteogenic function of the periosteum claimed, as had Goodsir, that the new bone was due to growth of adhering bone particles that remained attached in the process of removal from the cortex. Ollier attempted to meet this objection by examining the detached pieces of periosteum with a hand lens; and he stated that he could not find any osseous plaques on his detached pieces of periosteum. It is interesting to note that Ollier found the osteogenesis different in different animals, and even in different bones of the same or other animals. He was well aware of the fact that the periosteal graft from the rabbit had greater powers of reproduction than those from the cat; also, that a periosteal graft from the nasal bone of the cat would hold, while that from a similar bone of the rabbit would fail to do so. He found that the transplanted dura mater was more efficient in osteogenesis than the pericranium. He discovered that the osteoblasts were fewer in the deeper layers of the periosteum of old animals than in that of young animals, but that they could be increased by the stimulation of injury to the bone. An explanation of the discrepancies in the findings of early and recent investigations may be due in part to the differences in osteogenesis of different animals and bones as observed by Ollier. Ollier concluded from his studies on fractures that the periosteum formed the greatest amount of callus; the endosteal surface, a lesser amount; and the bone itself, the least. From his studies on the behavior of bone grafts, he determined that the most suitable material was a piece of living bone with both the periosteum and the marrow surface intact.

The chief discussion now shifted to the investigation of the bone graft. The main issues were concerned with the questions as to

7. Flourens, M. J.-P.: Recherches sur le developement des os et des dent, 1842.

8. Ollier, Louis: Traité experimental et clinique de la regeneration des os et de la production artificielle du tissu osseux, Paris **1** and **2**, 1867.

whether the graft lived after removal and transplantation, and the relationship of the periosteum to the graft. Just as two factions arose with regard to the function of the periosteum in bone growth and repair, so there were two schools with opposite views as to the importance of the periosteum to the bone graft. Barth [9] came forward with the statement that the entire graft died, and took no part in the regenerative changes. Later,[10] he admitted that the living periosteal covered bone was the best material for producing the stimulation of new bone.

Axhausen,[11] in 1908, published the results of his extensive experimental work. He came to the conclusion that the graft did live, and that the chief source of the living osteogenic cells was the periosteum and, to a lesser degree, the lining of the medullary cavity. Axhausen found that bone grafts without periosteum were much less viable than those with periosteum, although he admits that some results may be obtained with bare grafts.

A number of articles appeared in the few years subsequent, on the subject of bone transplants, a majority favoring the views of Ollier. With the publication of Macewen's [12] book "The Growth of Bone," attention was once more directed to the rôle of the periosteum in the regeneration of bone. Macewen recalled Goodsir's statement that the periosteum was merely a limiting membrane. He believed that any signs of osteogenesis were due to the presence of osseous tissue detached from the underlying cortex; and he presented additional experimental work and clinical facts to substantiate his contention. It is believed that Macewen has minimized the importance of the periosteum in just as great a degree as the proponents of the view that the periosteum is osteogenic have exaggerated that idea.

Almost simultaneously with the appearance of Macewen's book, in 1913, I published an article [13] entitled, "Regeneration of Bone from Periosteum," in which a number of experiments were reported showing that the periosteum had the power to regenerate bone. The importance of the other osteogenic areas were not given due consideration in this article.

In the following years, there were numerous articles, dealing with the regenerative power of the periosteum; in its normal position, as a

---

9. Barth, A.: Histologische Untersuchungen über Knochenimplantationen Beitr. z. path. Anat. u. z. allg. Path. **17**:64-143, 1896.

10. Barth, A.: Ueber Osteoplastik, Arch. f. klin. Chir. **86**:859, 1908.

11. Axhausen, Georg: Die histologischen und klinischen Gesetzder freien Osteoplastik auf grund von Thierversuchen, Arch. f. klin. Chir. **88**:23, 1908-1909.

12. Macewen, William: The Growth of Bone, Glasgow, James Maclehose & Sons, 1912.

13. Haas, S. L.: Regeneration of Bone from Periosteum, Proc. Soc. Exper. Biol. & Med. **10**:57-58, 1912; Surg., Gynec. & Obst. **17**:164-174 (Aug.) 1913.

free transplant, or in relation to a transplanted piece of bone. Even with the better facilities for working, convincing proof, for or against the osteogenesis of the periosteum, is still lacking. The question naturally arises as to what explanation can be made for differences in the conclusions of the various investigators. The observations of Ollier, on the difference in the osteogenesis of different animals, and even of different bones in the same animal, explains some of the discrepancies in the results. Furthermore, there is a greater activity of the osteogenic cells in the young animals than in the older animals, and this fact may lead to error in interpretation. A considerable amount of confusion has arisen over the exact definition of the periosteum, the addition of new terms and the arbitrary statements that neither can be proved or disproved. In the first place, the definition of the periosteum must be based on the histologic structure of that membrane. If one set of observers claim that the inner cellular layer of this membrane does not belong to the periosteum, while another group maintain that it does, there will be no uniformity of opinion until that point is settled. It would be just as logical to claim that any signs that osteogenesis was taking place on the outer surface of the bone were due to adherent active cells of the inner layer of the periosteum as it would be to assert that any signs of osteogenesis on the removed periosteum were due to adherent osseous plaques from the outer surface of the cortex. The removal of the periosteum is a surgical procedure, and one cannot submit the specimen to a histologic examination and at the same time to a physiologic test. Therefore, it is necessary to rely on the gross appearance for evidence of osseous tissue adhering to the periosteum. It is my opinion that, by the careful removal of the periosteum without the use of very sharp instruments, one can uniformily obtain specimens of periosteum free from osseous elements. In old animals, the periosteum is more firmly adherent, but there is a natural cleavage plane between it and the cortex. The cohesive force that exists between the structural components of the cortex is stronger than that between periosteum and cortex; so that there is not much chance of removing bone particles unless the bone is scraped with a sharp instrument. From the practical standpoint and in the routine practice of the surgeon, the periosteum is considered as that membrane which he strips away from the cortex. If this tissue is osteogenic, it is of prime importance to him, and he will use especial care to preserve it. The teaching, on the basis of unaccepted hair-splitting histologic investigations, that the periosteum is not osteogenic is wrong, and may be a source of harm. Fortunately, most of the surgeons who hold that the periosteum is not osteogenic advise that it be preserved for some other reason, such as its serving as a path for ingrowth of blood vessels.

The present investigation is concerned with determining the rôle played by the periosteum and endosteum in the healing of fractures in transplanted bone. The findings will naturally have an important bearing on the question of the behavior of the periosteum and endosteum in the growth and regeneration of bone, under usual condition, as well as in transplants.

TECHNIC EMPLOYED IN EXPERIMENTAL WORK

I wish to make clear what I consider periosteum and my method for its removal in experimental work. A longitudinal incision is made through the periosteum to the cortex. The membrane is then raised slightly with the sharp end of the scalpel, after which it is peeled off with the blunt end. In this way, one is reasonably certain of not removing any osseus particles with the periosteum. It might be stated at this time that it is not denied that osteoblastic cells capable of proliferation may remain on the outer surface of the cortex.

The removal of the endosteum can be accomplished only by curetting the medullary cavity. In so doing, the marrow and adjoining osseous tissue are taken away at the same time. A small curet or sharp hooked instrument was used for this purpose, the entire circumference of the marrow cavity being covered to a considerable distance back from the fracture surface.

The basic principle of this work is dependent on the fact that a fractured transplanted bone with both the periosteum and endosteum intact will heal even when placed in a muscle bed remote from any other osseous tissue.[14] A fractured bone when placed in muscle is in a most unfavorable environment because of the complete destruction of the original blood supply, the loss of osseous contact with normal bone and failure of functional stimulation. In other words, it is working at a very low threshold of physiologic stimulation, and therefore necessarily would be quite sensitive to any further injury, such as removal of the periosteum or the endosteum, or both.

Accordingly, the following series of experiments were performed on dogs, under general ether anesthesia, and with the usual aseptic technic. An entire metacarpal bone was removed from the foot and then completely fractured at the center. The periosteum was removed from both fragments in one series of experiments; the endosteum was curetted in another, and both the periosteum and the endosteum were curetted in the final series. The fragments were then placed in apposition and retained by a catgut suture, passed through two holes near the plane of fracture, or, when possible, wound over the ends. The bone

14. Haas, S. L.: Spontaneous Healing Inherent in Transplanted Bone, J. Bone & Joint Surg. 4:209-214 (April) 1922.

was reimplanted in its normal position or transplanted to the muscles of the back. At the end of a fixed period, the bones were removed and prepared for microscopic study.

REIMPLANTATION OF FRACTURED BONE AFTER REMOVAL OF THE PERIOSTEUM

EXPERIMENT 1.—*Operation.*—From Dog 1, a fully grown animal, the third metacarpal bone was removed and fractured at the center. The periosteum was stripped of the fragments, which after being placed in apposition were returned to their original position. The bone was removed in seventy-three days.

Gross Findings.—There was normal healing. At the site of fracture, there was a large knoblike mass of callus and fairly firm union. The roentgenogram revealed a large amount of callus at the site of fracture, which was not completely ossified.

Microscopic Findings.—There was a large amount of callus at the site of fracture, of both the osseous and the cartilaginous type. A complete osseous bridging between the fragments could not be demonstrated in the sections studied. The cortical bone contained both stainable and nonstainable nuclei, the latter being in the bone away from the site of fracture. The nuclei about the haversian canals were especially well stained.

EXPERIMENT 2.—*Operation.*—From Dog 22, a full grown animal, the third right metacarpal bone was removed and fractured in the middle. The periosteum was stripped off from the fragments, which were then restored to their normal position. The bone was removed at the end of ninety-four days.

Gross Findings.—There was no sign of union between the two fragments.

Microscopic Findings.—There was a small amount of new osteoid tissue on each fragment, but the two ends were separated by fibrous tissue. The new bone arose from the endosteal surface. There was union between a free particle of bone and the end of one fragment. The nuclei of the cortex, about the haversian canals, were well stained. The remainder were in various stages of degeneration. The outer surface of the bone showed marked signs of absorption.

EXPERIMENT 3.—*Operation.*—From Dog 4, a young animal, the third left metatarsal bone was removed and fractured in the center, and the periosteum was stripped off the cortex. The fragments were then fixed in normal apposition and reimplanted in their normal position. The bone was examined at the end of 116 days.

Gross Findings.—The fragments were found to be firmly united. There was a synosteosis with the adjoining metatarsal bone at the base, an opportunity being thus afforded for the ingrowth of normal bone. The roentgenogram showed the union to be complete (Fig. 1).

SUMMARY

In one of the three experiments, a firm union had occurred; while in another experiment, there was firm union in the gross, although on microscopic examination a continuous bridge of callus was not demonstrable, although it is possible that, in a complete serial section, a connecting bridge would have been found. In the other experiment, there was some osteoid tissue about the ends of the bone, although they were separated by fibrous tissue. Thus, it may be concluded that the removal of the periosteum will not prevent the union of a fracture in a reimplanted bone.

TRANSPLANTATION OF FRACTURED BONE AFTER REMOVAL OF THE PERIOSTEUM

EXPERIMENT 4.—*Operation*.—From Dog 22, a full grown animal, the fourth metatarsal bone was transplanted to the muscles on the right side of the back, after being fractured and having the periosteum removed. The bone was examined at the end of sixty-four days.

Gross Findings.—There was no sign of union and the fragments showed considerable evidence of absorption.

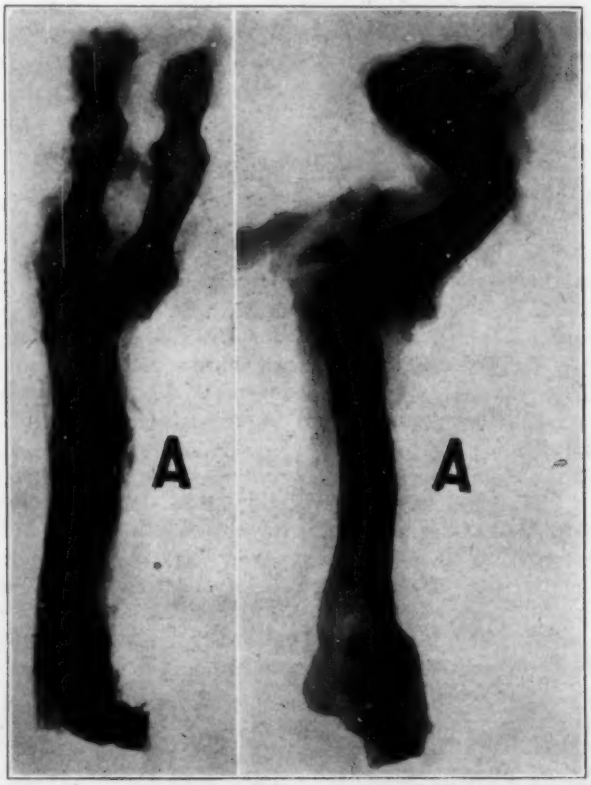

Fig. 1 (Exper. 3).—Reimplanted fractured bone, from which the periosteum had been removed. There was firm union at the end of 116 days. The line of fracture was just visible in the roentgenogram; *A*, plane of fracture.

Microscopic Findings.—One segment was found in a group of polymorphonuclear cells and appeared dead. The other fragment showed some evidence of osseous proliferation from the fracture surface.

EXPERIMENT 5.—*Operation*.—From Dog 19, a growing animal, the fourth metacarpal was removed, and the periosteum was taken off the shaft. The bone was then completely fractured, and the apposed fragments were transplanted to the muscles on the right side of the spine. The specimen was removed at the end of sixty-seven days.

Gross Findings.—There was firm union between the two fragments. The roentgenogram (Fig. 2) revealed a definite bridging of the gap between the bone ends with osseous tissue.

Microscopic Findings.—There was a definite osseous connection between the two fragments, on one side of the cortex. There was some cartilage scattered within the osseous callus. The cortex was stained fairly well, but showed marked evidence of absorption on the surface (Fig. 3).

EXPERIMENT 6.—*Operation.*—From Dog 1, a full grown animal, the fourth metacarpal was taken out, and the periosteum was removed from the shaft. The bone was then fractured at the middle, and the two fragments were transplanted to the muscles on the left side of the spine, in relatively normal contact. The bone was removed in seventy-three days.

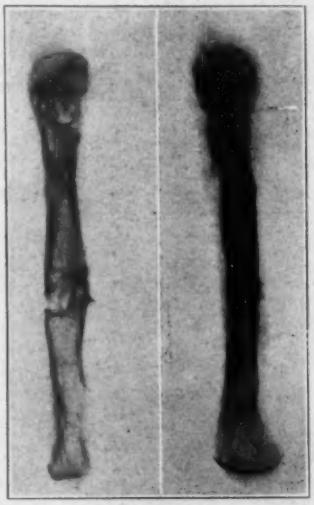

Fig. 2 (Exper. 5).—Transplanted fractured bone from which the periosteum was removed before being placed in the muscles of the back. There was firm union at the end of fifty-seven days. The roentgenogram taken in planes at right angles shows the site of fracture and union, the callus of which is not fully ossified.

Gross Findings.—Union had taken place between the two fragments. There was little excess callus and the bone had undergone considerable absorption. The roentgenogram revealed complete osseous union at the site of fracture.

Microscopic Findings.—There was complete osseous union at the site of fracture. The nuclei of the original bone stained poorly. The callus was mostly from the endosteal side. There was considerable absorption on the surface of the bone. The marrow appeared fairly normal.

EXPERIMENT 7.—*Operation.*—From Dog 12, a full grown animal, the third right metacarpal was removed and fractured at the center, and the periosteum was stripped off the fragments. The latter, after being put in apposition, were transplanted to the muscles on the right side of the spine, from which they were removed at the end of eighty-six days.

Gross Findings.—The alinement was good, but there was slight mobility at the site of the fracture.

Microscopic Findings.—There was an outgrowth of osteoid tissue from the ends of the bone, but bridging of the gap was incomplete. The new bone appeared to have arisen from the endosteum, and was not very thick. There were some normal stained nuclei about the end of the bone and about the haversian canals, but those of the remainder of the cortex were stainless.

EXPERIMENT 8.—*Operation.*—From Dog 12, a full grown animal, the fourth right metacarpal was removed and fractured at the center, after which the periosteum was stripped off the surface. The apposed fragments were then transplanted to the muscles on the right side of the spine, from which they were removed at the end of eighty-six days.

Fig. 3 (Exper. 5).—Site of union of fractured transplanted bone from which the periosteum had been removed. There was firm union in the gross at the end of fifty-seven days. The osteoid and cartilaginous callus may be noted; *A, A,* original cortex; *B, B,* cartilaginous and osseous callus.

Gross Findings.—There was no evidence of union of the two fragments.

Microscopic Findings.—There was extensive endosteal proliferation within the fractured end of one fragment, while the other was pointed and the marrow cavity completely enclosed by osseous tissue. There was marked evidence of absorption of the bone.

EXPERIMENT 9.—*Operation.*—From Dog 4, a young animal, the fourth metatarsal bone was removed and fractured in the middle, and the periosteum was taken off. The fragments were then bound together and transplanted to the muscles on the left side of the back, from which they were removed in 116 days.

Gross Findings.—The alinement of the bone was good, but there was a failure of union between the fragments. The roentgenogram revealed the separation at the site of the fracture.

Microscopic Findings.—The two ends were separated by a layer of fibrous tissue, although there were signs of proliferation and indications of an attempt to bridge the gap. There was considerable absorption on the surface.

SUMMARY

In two of the six experiments, a firm osseous union was found, and was verified by microscopic examination. In one other, there was union on gross examination, but a complete osseous bridge was not demonstrated in the microscopic preparation. In the remaining three experiments, there was a failure of union, although there was some proliferation from the ends.

It may be concluded that, under favorable conditions, union will take place in a fractured bone buried in muscle after removal of the periosteum.

REIMPLANTATION OF FRACTURED BONE AFTER REMOVAL OF THE ENDOSTEUM

EXPERIMENT 10.—*Operation.*—From Dog 21, which was almost full grown, the third left metacarpal bone was removed from the foot and broken completely at the center, and the medullary cavity was curetted. The apposed bones were then reimplanted in their normal position, and were removed at the end of thirty-three days.

Gross Findings.—The fragments were found overlapping, without any evidence of union.

Microscopic Finding.—There were several large masses of cartilaginous and osteoid callus arising from the periosteal surface at the site of fracture. In the cortex, there were some well-stained nuclei about the haversian canals, but the remaining nuclei were in various stages of degeneration.

EXPERIMENT 11.—*Operation.*—From Dog 13 the third right metacarpal bone was removed and fractured at the center. The endosteum was curetted from both fragments, after which the normal apposition was secured and the bone placed in its normal position. The specimen was removed at the end of ninety-five days.

Gross Findings.—There was firm osseous union between the two segments of bone. The roentgenogram (Fig. 4) revealed a complete periosteal callus connecting the two fragments. The central portion was not fully ossified. There was a synosteosis between the proximal fragment and the adjoining bone.

EXPERIMENT 12.—*Operation.*—From Dog 10, the fourth right metacarpal bone was removed and fractured at the center, leaving a strip of periosteum along one side. The endosteum was curetted away, and the two apposed fragments were reimplanted in their normal position, from which they were removed at the end of ninety-eight days.

Gross Findings.—There was angulation of the fragments and considerable mobility between the two ends. The roentgenogram revealed some periosteal callus and incomplete bridging of the gap.

Microscopic Findings.—There was some periosteal callus on the end of each fragment, between which there was a dense layer of fibrous tissue. There was no proliferation from the endosteal side and the cortical bone contained poorly stained nuclei.

SUMMARY

In one of the three experiments, there was firm union of the fragments. In the two other experiments, there was nonunion, but there was definite osseous callus at the ends of the bone, in the region of the periosteum. In the foot, there is always more chance for displacement of the segments. Thus, it may be concluded that, under favorable conditions, union will take place in reimplanted bones, after removal of the endosteum.

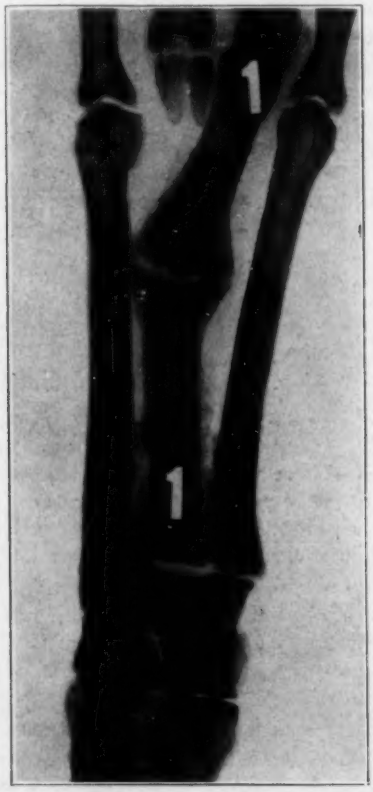

Fig. 4 (Exper. 11).—Reimplanted metatarsal bone, which was fractured and had the endosteum curetted away. There was very firm union on gross examination. The large periosteal callus, which is not completely ossified, may be note. *1, 1,* fragments of bone united by osseous and cartilaginous callus.

TRANSPLANTATION OF FRACTURED BONE TO MUSCLE OF THE BACK AFTER REMOVAL OF ENDOSTEUM

EXPERIMENT 13.—*Operation.*—From Dog 14, almost full grown, the fourth metacarpal bone was removed and fractured at the center, and the endosteum was curetted from each fragment. The segments were then fixed in normal apposition and transplanted to the muscles on the left side of the back, from which they were removed at the end of fourteen days.

Gross Findings.—There was good alinement of the fragments, but no sign of union.

Microscopic Findings.—There was no evidence of callus at either fracture surface, but a considerable amount of new osteoid tissue was found beneath the periosteum, along the outer surface of the cortex.

EXPERIMENT 14.—*Operation.*—From Dog 11, the third right metatarsal bone was removed and fractured at the center, leaving a strip of periosteum along one side. The endosteum was curetted, and the bones were placed in normal relation and then transplanted to the muscles on the right side of the back, from which they were removed at the end of fifty-eight days.

Gross Findings.—There was good alinement of the fragment, but a certain amount of play at the site of fracture. The roentgenogram revealed some

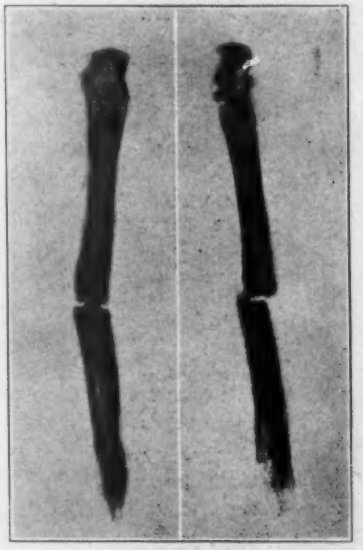

Fig. 5 (Exper. 14).—Transplanted metatarsal bone, which was fractured in the center, and the endosteum curetted out. There was union at the end of fifty-eight days when the bones were removed from the muscles of the back. The callus, which was not calcified, did not show well in the roentgenogram, but could be seen in the microscopic section (Fig. 6).

bridging of the gap, with a thin osseous layer in the region of the endosteum. There was slight absorption at the surface (Fig. 5).

Microscopic Findings.—There was a definite osseous connecting callus between the two segments on one side of the cortex. The remainder of the gap was filled with fibrous tissue. The cortical bone, for the greater part, with the exception of the region bordering on the haversian canals, contained poorly stained nuclei. There was some proliferation in the endosteum, back from the fractured surfaces (Fig. 6).

EXPERIMENT 15.—*Operation.*—From Dog 21, almost full grown, the fourth left metacarpal bone was removed and fractured in the middle, and the

endosteum was curetted from both segments. They were then placed in apposition and transplanted to the muscles on the left side of the spine. They were removed at the end of sixty-three days.

Gross Findings.—The fragments were found in good alinement and there appeared to be a soft uniting callus.

Microscopic Findings.—There was a large amount of osteoid callus at the site of fracture, but a complete connecting span could not be found in the sections studied. There was a connecting bridge of bone with a loose fragment on one side. The cortical bone was composed of poorly stained nuclei, and there was considerable absorption on the surface.

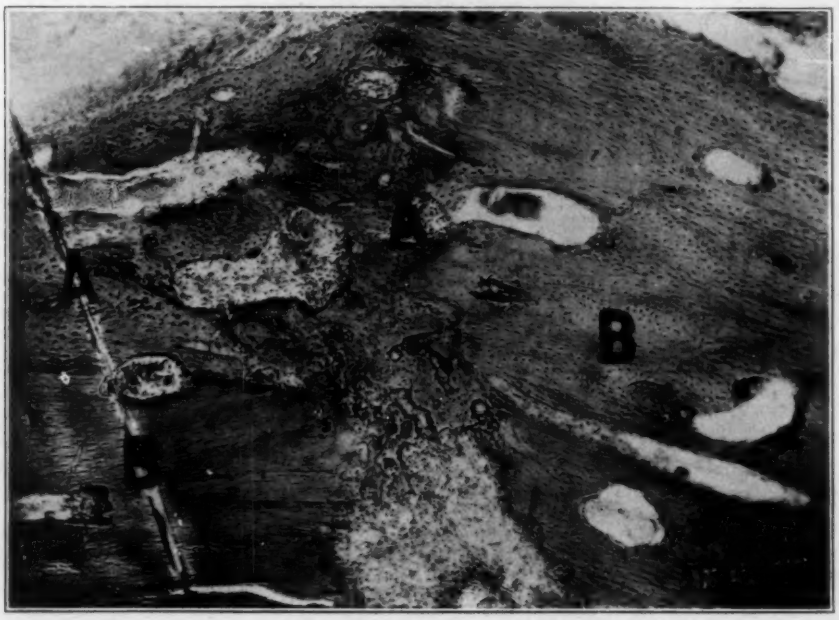

Fig. 6 (Exper. 14).—Photomicrograph of a section through the site of fracture of a transplanted bone from which the endosteum was curetted. At the end of fifty-eight days, there was union, on gross examination. Very little callus was shown in Figure 5, owing to the small amount of lime salts. The microscopic examination revealed a definite osteoid callus, arising chiefly from the periosteum, connecting the two fragments; *A, A,* osteoid callus; *B, B,* original cortex. (Occ., 2 inches; obj., ⅔ inch.)

Experiment 16.—*Operation.*—From Dog 18, a full grown animal, the third left metacarpal bone was removed and fractured at the center, and the endosteum was curetted out of both segments. The apposed fragments were placed in the muscles on the left side of the spine, from which they were removed at the end of sixty-seven days.

Gross Findings.—The fragments were found in good alinement, but there was some mobility at the site of junction. The roentgenogram revealed an apparent osseous union and marked absorption of the cortex.

Microscopic Findings.—There was a marked endosteal proliferation in one of the fragments. In spite of the osseous connection demonstrated in the roentgenogram, there was no osseous tissue between the two ends, in the microscopic sections. There were a considerable number of polymorphonuclear cells about one fragment.

EXPERIMENT 17.—*Operation.*—From Dog 10, not quite full grown, the fourth metatarsal bone was removed and fractured at the center, leaving a strip of periosteum along one side. The endosteum was curetted, and the two apposed fragments were placed in the muscles on the left side of the spine, from which they were removed in ninety-eight days.

Gross Findings.—There was definite osseous union between the two fragments, which was verified by the roentgenographic findings.

Microscopic Findings.—There was osseous callus connecting the two fragments. The nuclei of the adjoining cortex were poorly stained, and there was considerable absorption on the surface of the cortex.

SUMMARY

In two of the five experiments, there was definite osseous union between the transplanted fragments, in both the gross and the microscopic examination. In one other, there was apparent union, from the gross and the roentgenographic findings; but this was not verified by the microscopic study. Of the remaining two specimens, one showed considerable callus at the site of fracture, but the other showed no callus, on account of the short duration of the observation.

It may be concluded that the removal of the endosteum does not prevent union of a fracture in a transplanted bone, and that it interferes to a lesser degree than the removal of the periosteum.

REIMPLANTATION OF FRACTURED BONE AFTER THE REMOVAL OF BOTH THE PERIOSTEUM AND THE ENDOSTEUM

EXPERIMENT 18.—*Operation.*—From Dog 20, the third left metacarpal bone was removed and fractured in the middle. The periosteum was stripped off and the endosteum curetted, after which the two fragments were fixed together and reimplanted in their original position. The specimen was removed in eighteen days.

Gross Findings.—There was slight malalinement of the fragments, and no sign of union.

Microscopic Findings.—There was no sign of proliferation or formation of callus at the end of the bone. Some of the nuclei of the cortex were stainable, and some were not.

EXPERIMENT 19.—*Operation.*—From Dog 11, the third left metacarpal bone was removed and fractured at the center, and both the periosteum and the endosteum were taken away. The apposed fragments were replaced in their normal position. Duration of the experiment was fifty-eight days.

Gross Findings.—There was overlapping of the ends, and there were no signs of union. The roentgenogram revealed the condition of nonunion, and the presence of pointed fracture surfaces and a small mass of bone back from the site of fracture (Fig. 7).

Microscopic Findings.—The ends of the fragments were absorbed and showed no evidence of proliferation (Fig. 8). The nuclei of the cortex were stainless, except for a small nodule in the medullary canal, some distance back from the fracture line.

EXPERIMENT 20.—*Operation.*—From Dog 19, a full grown animal, the third right metacarpal bone was removed, the periosteum was taken off and the endosteum was curetted, after the bone was fractured in the middle. The segments were then placed and held in apposition, after which they were put in their original position. The specimen was removed in sixty-seven days.

Fig. 7 (Exper. 19).—Reimplanted fractured bone from which both the periosteum and endosteum had been removed. At the end of fifty-eight days, there was no sign of union. The ends of the bone at the site of fracture were pointed and the surface of the cortex showed evidence of absorption. *1, 1,* reimplanted fragments with nonunion and complete absence of callus.

Gross Findings.—The fragments were found in malposition, without any signs of union. The roentgenogram revealed failure of callus formation and absorption of the bone.

Microscopic Findings.—There was considerable cartilaginous and osseous callus at the ends of the fragments, but no signs of bridging of the gap. The cortex contained well stained nuclei, and there were numerous osteoblastic cells on the endosteal surface.

EXPERIMENT 21.—*Operation.*—From Dog 13, the third left metacarpal bone was removed and fractured in the middle. The periosteum and endosteum were removed, and the apposed fragments were replaced in their normal position, from which they were removed at the end of ninety-five days.

Gross Findings.—There was an angular deformity at the site of fracture, and definite mobility between the two fragments. The proximal segment had united with the adjoining bone at its base, and there was some irregularity at its fracture surface. The roentgenogram revealed the displacement of the fragments, and the presence of a slight amount of callus at the end of the proximal segment.

Microscopic Findings.—There was a marked osteoid proliferation at the end of one of the fragments, probably the proximal. The cortex was for the most part devoid of stainable nuclei. The other segment was without signs of proliferation, and for the greater part was undergoing absorption.

Fig. 8 (Exper. 19).—Photomicrograph of a section through the end of one of the segments of a fractured reimplanted bone, from which the periosteum and endosteum had been removed. The complete absence of callus and marked signs of absorption may be noted. *A, A,* fibrous tissue about end of fragments; *B, B,* original cortex with degenerated nuclei and complete absence of osteogenesis.

SUMMARY

There was a failure of union in all of the four experiments in which both the periosteum and endosteum were removed. In two of the experiments, there was evidence of proliferation, about the ends of the bone. In reimplantation, there is always the possibility of fusion with the adjoining bones, and ingrowth of new bone from that source.

It may be concluded that the removal of the periosteum and endosteum will prevent the union of a fracture in a reimplanted bone, although there may be some proliferation from the broken ends.

TRANSPLANTATION OF THE FRACTURED BONE TO MUSCLE AFTER REMOVAL OF THE PERIOSTEUM AND ENDOSTEUM

EXPERIMENT 22.—*Operation.*—From Dog 33, a full grown animal, the fourth left metacarpal bone was removed and fractured in the middle, and the periosteum and endosteum were taken away. The apposed fragments were transplanted to the muscles, on the left side of the back, from which they were removed at the end of fourteen days.

Gross Findings.—There was no sign of union.

Microscopic Findings.—There were no signs of proliferation about the fracture surfaces, and the bone appeared dead.

EXPERIMENT 23.—*Operation.*—From Dog 20, the fourth left metacarpal bone was removed and broken at the center. The periosteum was stripped off the cortex and the endosteum curetted away, after which the two fragments were fixed together and placed in the muscles on the right side of the back, from which they were removed at the end of eighteen days.

Fig. 9 (Exper. 24).—Transplanted fractured bone from which both the periosteum and endosteum had been removed. There was a complete failure of union and marked absorption of the fragments. The fragments were removed from the muscles of the back at the end of fifty-eight days.

Gross Findings.—There was no sign of union.

Microscopic Findings.—There was no sign of callus formation or proliferation at any place, and the nuclei appeared degenerated.

EXPERIMENT 24.—*Operation.*—From Dog 11, the fourth left metacarpal bone was removed and fractured at the center. The periosteum was stripped off and the endosteum curetted, after which the apposed fragments were transplanted to the left side of the back for fifty-eight days.

Gross Findings.—There was failure of union and considerable absorption of the bone. The roentgenogram (Fig. 9) revealed the condition of nonunion, failure of callus formation and absorption of the bone.

Microscopic Findings.—There was no sign of callus (Fig. 10), and the ends of the fragments were pointed as a result of the absorption. Back from the ends, in the medullary canal, there was some new bone; but nothing on the surface of the bone. In the removal of the endosteum, it was not possible to remove the part at a considerable distance from the end.

EXPERIMENT 25.—*Operation.*—From Dog 18, almost full grown, the fourth left metacarpal was removed and fractured at the center. The periosteum was stripped off and the endosteum curetted, after which the apposed fragments were transplanted to the muscles on the right side of the spine. The specimen was removed in sixty-seven days.

Gross Findings.—There was no sign of union of the fragments. The roentgenogram revealed the lack of union, failure of callus formation and absorption of the bone.

Microscopic Findings.—The ends of the bone showed absorption, and there was lack of proliferation. There was some new bone in the medullary canal, at a considerable distance within the bone. There was some proliferation on the surface of the bone, and regenerative changes about the haversian canals.

Fig.10 (Exper. 24).—Photomicrograph of a section through one of the segments of a fractured transplanted bone from which both the periosteum and endosteum were removed. At the end of fifty-eight days, there was complete failure of union and no evidence of callus; *A, A,* end of the fragment encapsulated by fibrous tissue; *B, B,* cortex with stainless nuclei.

EXPERIMENT 26.—*Operation.*—From Dog 32, a full grown animal, the fourth right metacarpal bone was removed and fractured at the center. The periosteum was stripped off and the endosteum curetted, after which the two fragments were placed in apposition, in the muscles on the right side of the spine. The specimen was removed in sixty-nine days.

Gross Findings.—There was no sign of union. One of the fragments had undergone almost complete absorption. There was no evidence of callus formation or proliferation at the site of fracture.

Microscopic Findings.—Both segments showed marked evidence of absorption. There was no new bone or cartilage on either fragment. Some of the nuclei were fairly well stained.

EXPERIMENT 27.—*Operation.*—From Dog 13, the fourth left metacarpal bone was removed and fractured in the center, and the periosteum and endosteum were taken away. The apposed bone segments were then transplanted to the muscles on the left side of the back, from which they were removed in ninety-five days.

Gross Findings.—The bones were found in good alinement, with some stability between the two fragments. The roentgenogram revealed some proliferation from one of the fragments, but there was absorption and erosion of the surface of the bone.

Comparison of Results of Healing of Fractures in Transplanted Bones

	Bones					
	Reimplanted			Transplanted		
	Duration, Days	Results	Percentages	Duration, Days	Results	Percentages
Periosteum and Endosteum Intact	33	Callus		33	Union	
	71	Union	Union, 60	33	Callus	
	71	Union	Callus, 20	71	Callus	Union, 70
	73	Negative	Negative, 20	71	Un on	Callus, 30
	116	Union		73	Union	
				73	Union	
				116	Union	
Periosteum Removed	73	Union		64	Callus	
	94	Callus	Union, 66	67	Union	
	116	Union	Callus, 33	73	Union	Union, 50
				86	Union	Callus, 33
				86	Negative	Negative, 7
				116	Callus	
Endosteum Removed	63	Callus		58	Union	
	95	Union	Union, 33	63	Callus	Union, 75
	98	Callus	Callus, 66	97	Union	Callus, 25
				98	Union	
Periosteum and Endosteum Removed	18	Negative	Union, 0	14	Negative	
	58	Negative	Callus, 50	18	Negative	
	67	Callus	Negative, 50	58	Negative	Union, 0
	95	Callus?		67	Negative	Callus, 14
				69	Negative	Negative, 85
				95	Callus	
				98	Negative	

Microscopic Findings.—There was a gap between the two fracture surfaces, which was filled with fibrous tissue. There was a considerable amount of new osteoid tissue about the end of one segment, and a lesser amount about the opposite fracture surface. This new bone appeared to bear some relationship to the haversian canals of the fracture surfaces. The remainder of the cortex was being absorbed.

EXPERIMENT 28.—*Operation.*—From Dog 10, almost full grown, the third right metacarpal bone was removed and fractured at the center. The periosteum was stripped off and the endosteum curetted, after which the apposed fragments were transplanted to the muscles on the right side of the back. The bone was removed in ninety-eight days.

Gross Findings.—The bone was found without signs of union or proliferation. The roentgenogram revealed the nonunion and lack of callus.

Microscopic Findings.—The fragments were separated by fibrous tissue. There was no sign of callus or even of proliferation about the bone ends, which were undergoing absorption. The nuclei of the cortical bone were degenerated.

SUMMARY

There was a failure of union in all of the seven experiments, in which the periosteum and endosteum were removed from a bone that was fractured and transplanted to the muscles of the back.

Except for one experiment, there were no signs of proliferation or callus formation about the bone ends, which were invariably pointed and showed marked evidence of absorption.

Removal of the periosteum and curettage of the endosteum deprive the bone of practically all of its osteogenic cells, thereby preventing regeneration and reparation in the transplanted bone.

COMMENT

In this last group of experiments, in which both the periosteum and the endosteum were removed, there was a failure of union in every fractured transplanted bone. In only one experiment in which the bone was placed in muscle was there any sign of callus.

The removal of the periosteum reduced the chances of union to a slight extent.

The removal of the endosteum caused no disturbance in the results of union.

The results indicate that the removal of either the periosteum or endosteum alone is without affect on the healing of fractures in transplanted bones; but the removal of the periosteum and endosteum together causes a complete cessation of proliferation at the fracture surfaces, and consequently a failure of union in every case.

CONCLUSIONS

1. A fracture in a transplanted bone from which the periosteum has been removed may unite, either when transplanted to the muscles of the back or reimplanted in its normal position.

2. A fracture in a transplanted bone from which the endosteum has been curetted may unite, either when transplanted to the muscles of the back or reimplanted in its normal position.

3. A fracture in a transplanted bone from which both periosteum and endosteum have been removed did not unite, either when transplanted to the muscles of the back or when reimplanted in its normal position.

4. The chief source of osteogenic cells, for the repair of a fracture in a transplanted bone, is from the osteoblasts of the periosteum and the endosteum. The presence of either is sufficient for union. The periosteum plays a relatively more active part than the endosteum.

5. The explanation of those cases of nonunion not due to mechanical tissue interference or gross malpositions must be sought for in the factors that inhibit osteogenesis simultaneously in both the periosteum and the endosteum.

6. In order to attain a maximum of reparative power for any bone lesion, it is deemed essential to preserve the integrity of both the periosteum and the endosteum.

STUDIES IN EXHAUSTION: VI. SEPTICEMIA

G. W. CRILE, M.D.
CLEVELAND

An animal or a man who has first been exhausted by exertion, emotion, hemorrhage, asphyxia, anesthesia or loss of sleep succumbs more readily to infection, and an animal or a man exhausted by infection succumbs more readily to trauma, emotion, anesthesia, exertion, loss of sleep, etc. It becomes of value, therefore, to determine whether the exhaustion which is one of the phenomena of either an acute or a chronic infection is essentially different from exhaustion from other causes—emotion, exertion, physical trauma, insomnia.

In an attempt to answer this query, the following studies were made.

A. HISTOLOGIC STUDIES

I. The Histologic Effect of Bacteria or of Bacterial Toxins

Nichols, in 1899, Marinesco and other observers have demonstrated the presence of histologic changes in the central nervous system after death from typhoid fever or other diseases of infectious origin; and in inoculated animals. As in the preceding sections of these studies, however, the limited space at our disposal prevents a review of the literature, which has been constantly consulted throughout the progress of these researches.

DIPHTHERIA TOXIN

In this group of experiments, the protocols of which are given in Tables 1 and 2, intravenous injections of diphtheria toxin (Parke Davis & Co.) were given to rabbits in doses varying from a little less than the lethal dose to twice that amount. The length of life after the injection varied, as is shown in the tables, from four hours to two days.

PYOGENIC INFECTION

Experiment 1.—The development of a pyogenic infection in an animal in the laboratory provided an opportunity to observe its histologic effects.

Histologic Examination.—Cerebrum: There were some active cells; many fatigued, and some exhausted.

Cerebellum: Numerous hyperchromatic and active cells were found; and many fatigued (Fig. 1).

Spinal cord: All cells were active; none hyperchromatic, and none fatigued.

Liver: A slight loss of cytoplasm was noted in some cells; no congestion nor invasion of pus cells.

Suprarenal: There was very marked loss of cytoplasm in the outer two thirds of the cortex. The medulla was pale, with loss of chromaffin.

TABLE 1.—*Histologic Effects of the Injection of Diphtheria Toxin (Length of Life from Four to Fourteen Hours)**

Exper.	Experimental Data	Cerebrum	Cerebellum	Liver	Suprarenals	Other Organs and Tissues
1	Rabbit: weight, 2.202 kg.; killed 4 hours after injection of lethal dose, 0.55 c.c.)	.....	All Purkinje cells fatigued and exhausted	Considerable loss of cytoplasm in all cells; nuclear stain not bright	Entire cortical area showed uniform loss of cytoplasm; no nuclear changes; medulla normal	
2	Rabbit: weight, 1.480 kg.; killed 4 hours after injection of 0.21 c.c. (L = 0.37 c.c.)	.....	All cells fatigued and exhausted	.....	Slight uniform loss of cytoplasm of cells of cortex, except in outer layer, where cells are normal; medulla normal	
3	Rabbit: weight, 1.618 kg.; killed 4 hours after injection of lethal dose, 0.4 c.c.	An occasional hyperchromatic cell; most all fatigued; granules deeply stained	Most cells hyperchromatic; some fatigued; granules sharply defined	Vacuolation and great loss of cytoplasm in most of the cells	Marked loss of cytoplasm in many cortical cells	Thyroid: Much colloid; epithelium flat, no marked increase in interstitial tissue Kidney: Glomeruli normal; a few tubules showed complete desquamation, some very lightly stained
4	Rabbit: weight, 2.080 kg.; killed 4 hours after injection of 0.4 c.c. (L = 0.52 c.c.)	Most cells hyperchromatic, some fatigued	Many hyperchromatic cells; some fatigued and exhausted	Slight uniform loss of cytoplasm	Marked loss of cytoplasm in most of the cortical cells; medulla hyperchromatic	Spinal Cord: Anterior horn cells deeply stained; granules large and distinct Pancreas: Zymogen granules limited to basal part of cell; stain deep Spleen: Normal Voluntary Muscle: Normal Kidney: Glomeruli normal; many of the convoluted tubules stained faintly; some completely eroded and disintegrated
5	Rabbit: weight, 2.878 kg.; died 13 hours after injection of 1.4 c.c., twice the lethal dose	.....	Most cells active; some fatigued	No vacuolation but no distinct granules; stained with difficulty	Loss of cytoplasm in all cortical cells, vacuolation in some; outlines distinct; medulla normal	
6	Rabbit: weight, 1.688 kg.; died 14 hours after injection of 0.84 c.c., twice the lethal dose	An occasional hyperchromatic and active cell; many cells fatigued; some exhausted	All cells fatigued or exhausted	Loss of cytoplasm and vacuolation of some cells; remainder hyaline in appearance; nuclei well stained and central	Marked loss of cytoplasm and vacuolation in all cortical cells; medulla fairly well stained, with but little loss of cytoplasm; both cortex and medulla greatly congested	Spinal Cord: Anterior horn cells active Thyroid: Colloid in large acini, epithelium flat; no interstitial tissue Kidney: Normal glomeruli and tubules with striated epithelium; very marked congestion Heart: Normal; no pigmentation: well stained striations and nuclei Voluntary Muscle: Normal; striations clear Lung: Congested and collapsed Spleen: Normal except for marked congestion Testicle: Normal and well stained

* Experiments by A. F. Rowland; histologic examination by Drs. J. B. Austin and F. W. Hitchings.

* Experiments by A. F. Rowland; histologic examination by Drs. J. B. Austin and F. W. Hitchings.

TABLE 2.—*Histologic Effects of the Injection of Diphtheria Toxin* *

Exper.	Experimental Data	Cerebrum	Cerebellum	Spinal Cord	Liver	Suprarenals
1	Rabbit: weight, 1.890 kg.; killed 55½ hours after injection of 0.5 c.c. (L = 0.47 c.c.)	No hyperchromatic cells; some active cells; nearly all fatigued	Some hyperchromatic and active cells; many fatigued cells; a few exhausted	.....	Great loss of cytoplasm and some vacuolation in all cells	
2	Rabbit: weight, 1.935 kg.; died aproximately 53½ hours after injection of 0.5 c.c. (L = 0.48 c.c.)	No hyperchromatic or active cells; all badly fatigued or exhausted	An occasional hyperchromatic or active cell; most of the cells fatigued, some exhausted	Some fatigued cells in anterior horn	Loss of cytoplasm and vacuolation throughout; granuloma structure of cytoplasm lost	Outer two thirds of cortex shows congestion and hyaline or granular degeneration; medulla pale but no loss of cytoplasm
3	Rabbit: weight, 2.485 kg.; died approximately 40 hours after injection of 0.5 c.c. (L = 0.62 c.c.)	No hyperchromatic cells; many active or fatigued; an occasional exhausted cell	An occasional hyperchromatic or active cell; most of the cells fatigued, some exhausted	.....	Great loss of cytoplasm and vacuolation in all cells; cytoplasm markedly degenerated	Slight loss of cytoplasm throughout cortex, especially in middle third
4	Rabbit: weight, 1.730 kg.; died 46 hours after injection of 0.5 c.c. (L = 0.43 c.c.)	Many hyperchromatic and active cells; an occasional fatigued cell	An occasional hyperchromatic and active cell; many cells fatigued, some exhausted	.....	Great loss of cytoplasm and vacuolation; large degenerated areas	Slight loss of cytoplasm and degenerative changes in some areas of the middle third of the cortex; medulla normal
5	Rabbit: weight, 1.700 kg.; died 43 hours after injection of 0.5 c.c. (L = 0.42 c.c.)	Some hyperchromatic cells; nearly all active; a few fatigued	A moderate number of hyperchromatic and active cells; majority fatigued; some exhausted	Cells of the anterior horn hyperchromatic	Moderate loss of cytoplasm and slight vacuolation in all cells; most of the nuclei central	Slight loss of cytoplasm in outer one half of cortex; no vacuolation; medulla pale but no loss of cytoplasm

* Experiments by Dr. W. B. Rogers; histologic examination by Dr. J. B. Austin.

Kidney: Glomeruli and Bowman's capsule were normal. Marked cloudy swelling and degeneration of all tubules were present.

Thymus: The lymphoid tissue was compact; Hassall's corpuscles were small and numerous.

Submaxillary gland: Many mucous cells were vacuolated; very few granules were found in serous cells.

Spleen: Compact lymphocytes were found and there were some polymorphonuclear leukocytes in blood vessels.

Parotid gland: There was no less of substance, but the granules of the cells were not distinct.

Intestine: This was normal.

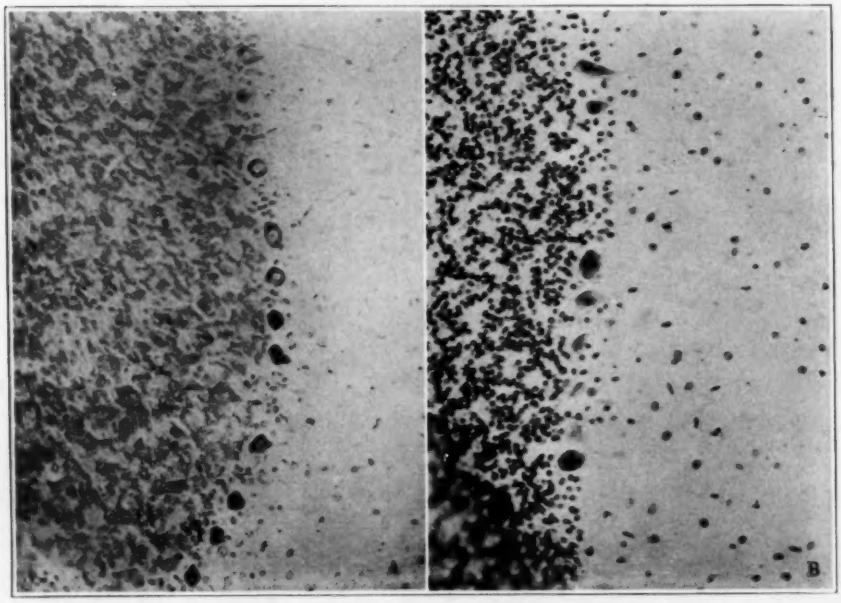

Fig. 1.—Effect of acute infection on the brain cells; *A*, section of the cerebellum of a normal cat; *B*, section of cerebellum of a cat infected with Streptococcus pyogenes (reduced from photomicrographs × 310).

Experiment 2.—Acute postoperative peritonitis occurred in a dog in which an intestinal anastomosis had failed to hold. The dog died on the third day and sections were taken immediately.

Histologic Examination—Cerebrum: There were no hyperchromatic cells, only a few containing any large granules. The cytoplasm was vacuolated in almost all cells. No chromatin was found in the nuclei. In many cells, only the nucleolus was present.

Cerebellum: A differential count of 100 Purkinje cells was as follows: active cells, 51 per cent. (normal dog count, 71.2); fatigued cells, 32 per cent. (normal, 28.1); exhausted cells, 17 per cent (normal, 0.7).

Medulla: Sections from the level of lower motor decussation showed most cells of the anterior horn markedly hyperchromatic, but early stages of fatigue in

some, and none of the cells markedly exhausted; in the posterior horn, few hyperchromatic cells, most of the cells showing more fatigue than those of the anterior horn. Most of the commissural cells were hyperchromatic, some exhausted.

Spinal cord: In the cervical region, most of the cells were hyperchromatic, especially the larger cells of the anterior horn. None of the ganglion cells contained large granules of chromatin. In many areas, cells contained no granules. In the lumbar region, all cells were greatly shrunken; some were hyperchromatic; the granules were small and few in number; the nucleoli were intact; the nucleoplasmar relation was disturbed. There were no exhausted cells, but many in the last stages of fatigue.

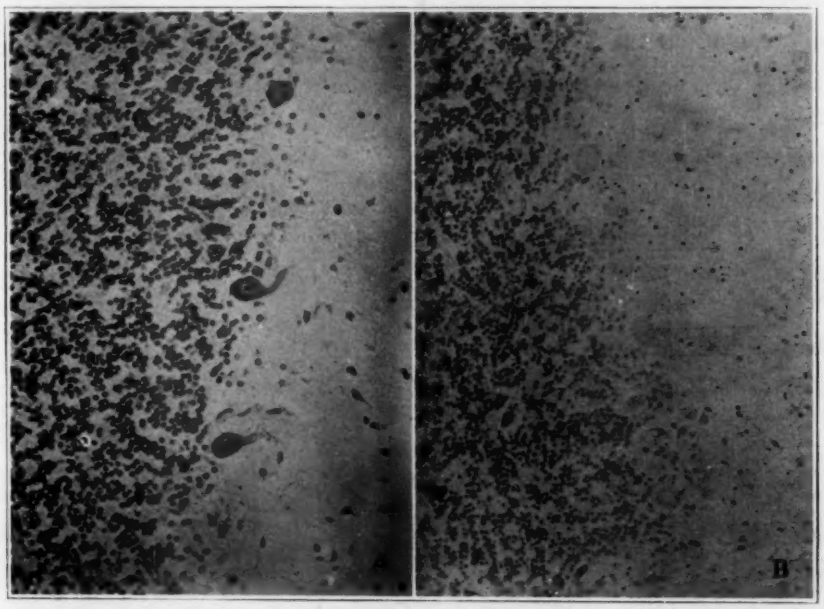

Fig. 2.—Effect of acute septicemia on the human brain; *A*, section of normal human brain; *B*, section of human brain after death from acute septicemia (reduced from photomicrographs × 310).

Tetanus Toxin.—Experiment 1.—Thirty-eight cubic centimeters of tetanus toxin was given to a dog (weight 3.205 kg.) intraperitoneally in repeated doses. The dog died five days later. Sections were taken immediately after death.

Histologic Examination.—Cerebrum: Most of the cells were fatigued; the capillaries were injected.

Cerebellum: There was an occasional hyperchromatic and active cell; but most all of the cases were fatigued.

Liver: The cytoplasm was uniform, but stained with difficulty; the capillary was deeply injected.

Suprarenal: There was slight loss of cytoplasm in some cortical cells.

Kidney: Glomeruli and capsule were normal; tubules, hyaline in appearance; cells, not striated.

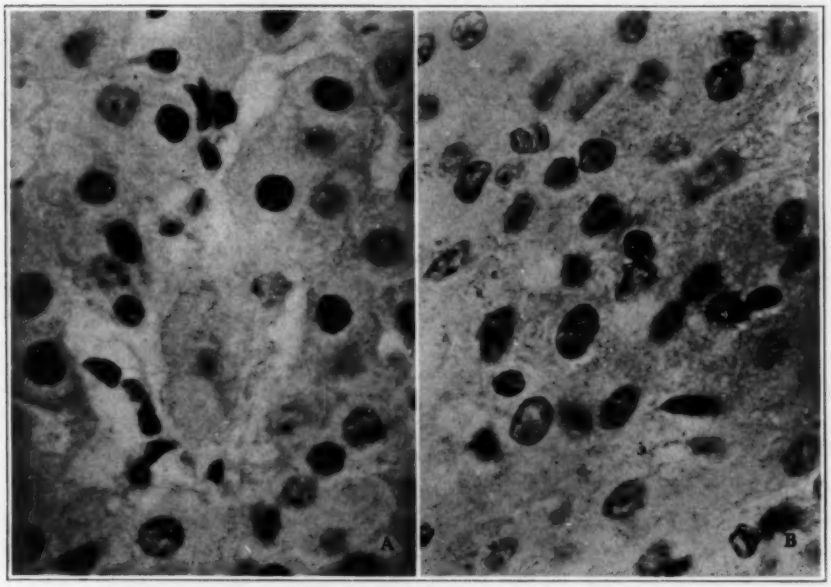

Fig. 3.—Effect of acute septicemia on the human liver; *A*, section of normal human liver; *B*, section of human liver after death from acute septicemia (reduced from photomicrographs × 1,640).

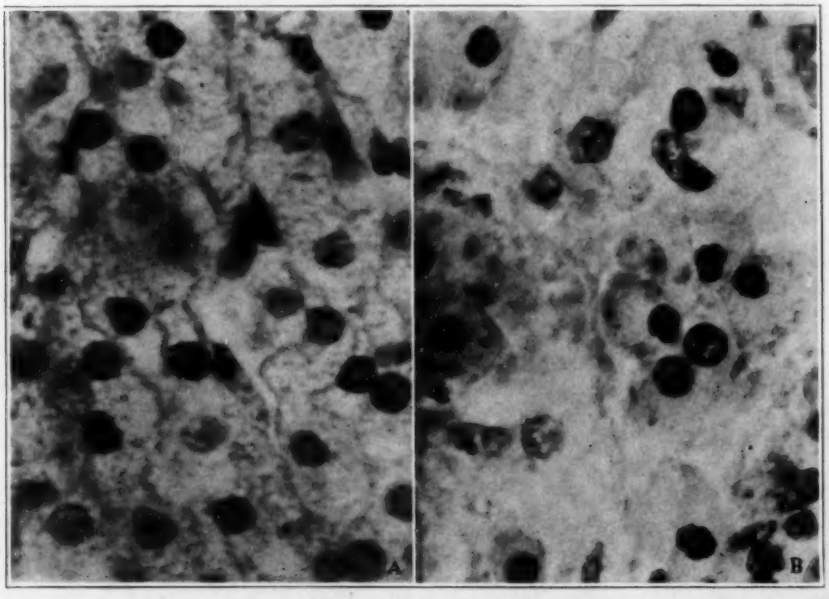

Fig. 4.—Effect of acute septicemia on the human suprarenals; *A*, section of normal human suprarenal; *B*, section of human suprarenal after death from acute septicemia (reduced from photomicrographs × 1,640).

Heart muscle: This was normal. Striations were faint; fibrillae were plain.

Voluntary muscle: Some areas were entirely normal. There was degeneration in others with no markings present.

Stomach: This was not well stained but was normal.

Thyroid: The acini were well filled with colloid; the epithelium was flat.

Spleen: This was normal.

PHYLACOGENS

In a group of experiments, animals were killed at varying periods after the intravenous injection of different phylacogens. The primary purpose of these experiments was to measure the suprarenal output, and detailed histologic examinations were not made. In most instances, however, the cerebellum was examined. These examinations, as is

TABLE 3.—*Histologic Effect on the Cerebellum of the Injection of Phylacogens* *

Experiment	Experimental Data	Length of Life After Injection	Histologic Appearance of Cerebellum
1	Dog: Ether anesthesia; gonorrhea phylacogen, intravenous, 2 c.c.	20 minutes	Active cells, 85%; hyperchromatic and fatigued cells, 15%; exhausted cells, 0
2	Dog: Ether anesthesia; mixed infection phylacogen, intravenous, 2 c.c.	25 minutes	Hyperchromatic and fatigued cells
3	Dog: Ether anesthesia; mixed infection phylacogen, intravenous, 2 c.c.	30 minutes	Hyperchromatic and fatigued cells
4	Cat: Ether anesthesia; gonococcus endotoxin, intravenous, 1 c.c.	30 minutes	Hyperchromatic
5	Cat: Gonorrheal phylacogen, subcutaneous, 6 c.c.; 30 minutes later, 2 c.c.; 43 minutes later, 2 c.c.	56 minutes after first injection	Hyperchromatic
6	Cat: Gonorrheal phylacogen, subcutaneous, 6 c.c.; 30 minutes later, 2 c.c.; 43 minutes later, 2 c.c.	1 hour 6 minutes after first injection	Hyperchromatic and fatigued
7	Rabbit, weight, 2 kg.: Gonorrheal phylacogen, intravenous, 4 c.c.	8 hours	Fatigued and exhausted
8	Rabbit, weight, 1.8 kg.: Gonorrheal phylacogen, intravenous, 4 c.c.	8 hours	Fatigued and exhausted

* Experiments by Drs. F. W. Hitchings and J. B. Austin.

shown in Table 3, demonstrate that the immediate effect is a hyperchromatic condition of the brain cells followed by a progressive approach to stages of diminishing activity and to fatigue in proportion to the length of time between the injection and the death of the animal.

We are indebted to Dr. F. W. Hitchings for the collection of the data regarding the following clinical cases of infection and to Dr. J. B. Austin for the histologic examinations (Figs. 2 to 4).

CLINICAL CASES

CASE 1.—*Acute streptococcus infection.* A man, aged 48, scratched his left hand twenty-four hours before he entered Lakeside Hospital. Examination revealed an acute infection with intense swelling, redness and tenderness which involved the left hand and arm and the right knee. Blood cultures were positive for streptococcus. Multiple incisions were made and the usual treatment was

followed. On entrance, the temperature was 104.6 F. Delirium developed, and just before death, twenty-four hours after admission, the temperature rose to 106.4 F.

The necropsy was made one hour postmortem. The pathologic diagnosis was acute septicemia, pulmonary and cerebral edema, colloid goiter and chronic endocarditis.

Histologic Examination.—Cerebrum: No hyperchromatic cells were found. As a whole, the cells seemed to be swollen rather than shrunken, as were their nuclei also. The nucleoli were usually present and were well stained, although in some cells the staining was faint and the nucleolus disintegrated. The small pyramidal cells were more affected than the large. On restaining after fixation in 96 per cent. alcohol, there was more cell shrinkage than in the preceding sections, but otherwise the changes were essentially the same.

Cerebellum: The cell changes were marked. A casual examination gave the impression that all of the cells were fatigued or exhausted, but this was confirmed only in part by the differential count of 100 Purkinje cells, which was as follows: active cells, 11 per cent. (normal human count,[1] 82; fatigued cells, 59 per cent. (normal, 16); exhausted cells, 30 per cent. (normal, 2).

CASE 2.—*Acute postoperative septicemia from Staphylococcus pyogenes-aureus.* A woman, aged 36, apparently about two months pregnant, on whom a vaginal repair operation was performed for laceration of the perineum, made an uneventful recovery from the operation as far as local symptoms were concerned. On the fourth day, it was noticed that her face was swollen on the right side behind the angle of the jaw. Her face continued to swell and became edematous, and a marked parotitis developed, with a temperature ranging from 99 to 104.3 F. just before death. She did not respond to treatment, and death occurred on the eighth day after operation. Previous to this time, the blood culture showed the presence of *Staphylococcus pyogenes-aureus.*

At necropsy, the following pathologic diagnosis was made: postoperative suppurative parotitis; acute cardiac dilatation; acute congestion of the spleen; cloudy swelling and passive congestion of the kidneys and liver; petechial hemorrhages into the spleen, medulla oblongata and pelvis of the kidney; retained placenta after a previous abortion; mild interstitial nephritis; chronic pleuritis; fetal adenoma of the thyroid gland, and acute endometritis decidualis.

Histologic Examination.—Cerebellum: A differential count of 100 Purkinje cells was as follows: active cells, 18 per cent. (normal human count, 82); fatigued cells, 60 per cent. (normal, 16); exhausted cells, 22 per cent. (normal, 2).

CASE 3.—*Paratyphoid fever.* A man, aged 30, who was admitted to Lakeside Hospital after being ill for three weeks, had neither headache or vomiting and very little cough. A diagnosis of paratyphoid fever was made, and was confirmed by the bacteriologic findings. The patient died nine days after entering the hospital.

At necropsy, there were found thrombosis of the left pulmonary artery, pulmonary infarction, hypostatic pneumonia, phlebitis of the femoral vein, ulceration of the ileum, acute parenchymatous nephritis with marked passive congestion, fatty changes in the liver and a healed pulmonary tuberculosis.

---

1. It is difficult to secure normal human brain tissues; but several cases of sudden death in apparently normal men supplied material for an approximate basis for a human standard of comparison.

Histologic Examination.—Cerebellum: A differential count of 100 Purkinje cells was as follows: active cells, 59 per cent. (normal human count, 82); fatigued cells, 29 per cent.; (normal, 16); exhausted cells, 12 per cent. (normal, 2).

CASE 4 (Presented through the courtesy of Dr. H. G. Sloan).—*Tetanus following an injury necessitating the amputation of both legs.* The patient had been run over by a railroad train. Although he was in profound shock, Dr. Sloan found it necessary to amputate both legs under spinal anesthesia, following the operation with a transfusion. The patient recovered from the operation and made good progress until the ninth day. Then symptoms of tetanus appeared and while antitoxin was at once given by injection into the spinal canal, opisthotonos, risus sardonicus, fever and convulsions were followed by death from respiratory failure, six days later.

Histologic Examination.—Cerebellum: In most of the cells, chromatin was present in large granules. Vacuolization of the nucleoli was noted in practically all the cells.

A differential count of 100 Purkinje cells was as follows: active cells, 22 per cent. (normal, human count, 82); fatigued cells, 49 per cent. (normal, 16); exhausted cells, 29 per cent. (normal, 2).

CASE 5.—*Chronic infection; empyema.* A man, aged 58, was admitted to Lakeside Hospital in a critical condition due to a severe empyema and long neglect. The infection became generalized, and death occurred nine days later.

The necropsy findings were chronic pleuritis, acute purulent pleuritis and pericarditis, and chronic myocarditis, nephritis, cystitis and gastritis.

Histologic Examination.—Cerebrum: The cells were greatly shrunken, and were surrounded by large vacuoles. In the few cells that were hyperchromatic, there were many large chromatin granules. Many of the Hodge type of cells were present; i. e., cells which were apparently shrunken hyperchromatic cells. They appeared as small masses of blue material. A second set of sections had practically the same appearance.

Cerebellum: A differential count of 100 Purkinje cells was as follows: active cells, 34 per cent. (normal human count, 82); fatigued cells, 53 per cent. (normal, 16); exhausted cells, 13 per cent. (normal, 2).

Medulla: The chief characteristic of the sections was the scarcity of nerve cells. In one of the medullary nuclei, hyperchromatic cells were present; while in other areas the chromatin was diminished in amount. Considerable pericellular vacuolization was present.

These histologic studies show that infection by the toxins of bacteria or by direct bacterial invasion produces characteristic histologic changes, which are most constantly present and are most marked in the brain, and in the cortex of the suprarenal, and are less marked in the liver in earlier stages of the infection. Marked changes in the liver appear in the later stages of infection.

The first effect of the injection of a toxin, as is shown by the early results of the injection of phylacogens, is to produce hyperchromatism of the brain cells. This is indicated also by the frequent appearance of hyperchromatic cells in the brains of the animals killed four hours after the injection of diphtheria toxin.

II. The Histologic Effects of the Injection of Bacterial Toxins in the Presence of Depressants of the Central Nervous System

DIPHTHERIA TOXIN AND MORPHIN

Two groups of experiments were performed, one in which large doses of morphin were administered before the injection of diphtheria toxin; another in which successive doses of morphin followed the injection of the toxin.

A comparison of the findings as shown in Tables 4 and 5 with those in Table 1 demonstrates that the effect of morphin was to reduce markedly the histologic changes in the brain, liver and suprarenals, the condition of these tissues being better in the animals in which the administration of morphin followed the injection of the diphtheria toxin (Figs. 5 to 7).

ETHER AND NITROUS OXID

In four instances, diphtheria toxin was administered to an animal under full ether anesthesia; in another instance, to an animal under full anesthesia with nitrous oxid. In each case, the anesthesia was continued for four hours, at the end of which period the animals were killed. The histologic findings are given in Table 6 (Figs. 8 to 10).

III. The Histologic Effects of the Injection of Diphtheria Toxin in a Decapitated Animal

The uniformly striking histologic changes in the cortex of the suprarenals following the injection of diphtheria toxin led to an attempt to discover whether or not the lesions in the suprarenals or those in the brain were the primary lesions.

Experiment.—A dog, weight 5.7 kg., was decapitated, the blood volume being maintained during the dissection by transfusion from another dog. Artificial respiration was supplied as soon as the dissection was completed. Ten cubic centimeters of diphtheria toxin was administered intravenously—a large lethal overdose (L = 0.25 c.c. per kilogram). The dog was killed thirty minutes after the injection.

Histologic Examination.—Liver: The stain was faint. There was no vacuolation, but there was infiltration of leukocytes around the blood vessels.

Suprarenals: The cortex and medulla were well stained and normal.

Pancreas: This was well stained. Not much zymogen material was present. Islands were large and few.

Voluntary muscle (cross section): The fibers were faint and not well differentiated. There were no distinct fibrillae. The nuclei were well stained.

The normal histologic appearance of the suprarenals is significant.

TABLE 4.—*Histologic Effects of Diphtheria Toxin Preceded by Morphin* *

Exper.	Experimental Data	Cerebrum	Cerebellum	Liver	Suprarenals	Other Organs and Tissues
1	Rabbit: weight, 1.903 kg.; subcutaneous injection of 2 gr. (130 mg.) of morphin sulphate followed in 1 hour by 3 gr. (195 mg.) intravenously 10 minutes after 2d dose; respiration, 24; lethal dose,0.47 c.c. diphtheria toxin intravenously; killed 4 hours later	Hyperchromatic and fatigued cells; none exhausted	.....	Slight uniform loss of cytoplasm; nuclear stain sharply defined	No loss of cytoplasm or vacuolation in cortex; medulla pale with loss of cytoplasm	
2	Rabbit: weight, 1.973 kg.; morphin sulphate given as in Experiment 1; 7 minutes after 2d dose, respiration, 76; lethal dose, 0.47 c.c. diphtheria toxin intravenously; killed 4 hours later	.....	Nearly all Purkinje cells hyperchromatic	Cells normal, full of zymogen	Normal; no loss of cytoplasm from cortical cells; medulla not deeply stained	
3	Rabbit: weight, 2.063 kg.; morphin sulphate as in Experiment 1; 15 minutes after 2d dose, respiration, 20; lethal dose, 0.50 c.c. diphtheria toxin intravenously; killed 4 hours later	.....	Many hyperchromatic cells; some fatigued	No loss of cytoplasm	Cortical cells all in good condition; medulla hyperchromatic	
4	Rabbit: weight, 1.420 kg.; intravenous injection of 20 mg. morphin sulphate, followed in 10 minutes by intravenous injection of 0.4 c.c. diphtheria toxin (L = 0.35 c.c.); killed 4 hours later	An occasional hyperchromatic cell; many fatigued cells	Many hyperchromatic cells; an occasional fatigued cell	Cells present homogeneous appearance; no loss of cytoplasm; nuclei well stained and normal	Marked loss of cytoplasm of most cells of cortex; medulla deeply stained	Kidney: Glomeruli normal; many tubules entirely desquamated; a few hyaline in appearance Thyroid: Much colloid; epithelium flat; no increase in interstitial tissue Spleen: Much hematogenous pigment; otherwise normal
5	Rabbit: weight, 2.0 kg.; intravenous injection of 20 mg. morphin sulphate, followed in 10 minutes by intravenous injection of 0.4 c.c. diphtheria toxin (L = 0.5 c.c.); killed 4 hours later	Hyperchromatic	Numerous hyperchromatic cells; many fatigued	Much loss of cytoplasm around central vein	Normal; no loss of cytoplasm; medulla deeply stained	Spleen: Normal

* Experiments and histologic examinations by Drs. J. B. Austin and F. W. Hitchings.

TABLE 5.—*Histologic Effects of Diphtheria Toxin Followed by Morphin* *

Exper.	Experimental Data	Cerebrum	Cerebellum	Liver	Suprarenals	Other Organs and Tissues
1	Rabbit: weight, 2.068 kg.; twice lethal dose, 1 c.c., diphtheria toxin followed by subcutaneous injections of morphin sulphate at successive intervals, as follows: 0 hr. 18 min., 30 mg.; 3 hr. 47 min., 40 mg.; 2 hr. 29 min., 40 mg.; 2 hr. 21 min., 60 mg.; 3 hr. 57 min., 40 mg.; total morphin, 210 mg.; died 18 minutes after last morphin injection; 13 hr. 10 min. after diphtheria toxin	.....	Most cells hyperchromatic; some active cells, very few fatigued	No loss of cytoplasm or vacuolation; no distinct granules; diffuse stain	Slight loss of cytoplasm without vacuolation in cortex; medulla normal	
2	Rabbit: weight, 2.398 kg.; twice lethal dose, 1.1 c.c., diphtheria toxin followed by subcutaneous injections of morphin sulphate at successive intervals as follows: 0 hr. 21 min., 30 mg.; 3 hr. 46 min., 40 mg.; 2 hr. 28 min., 40 mg.; 2 hr. 4 min., 40 mg.; 4 hr. 6 min., 40 mg.; 2 hr. 13 min., 40 mg.; total morphin, 230 mg.; died 52 minutes after last morphin injection; 15 hr. 50 min. after diphtheria toxin	Many hyperchromatic and active cells; some fatigued and exhausted	Most cells hyperchromatic and active; an occasional fatigued cell	Loss of cytoplasm and vacuolation in almost all cells	....	Spinal Cord: All cells hyperchromatic or active Thyroid: Small; colloid in large masses; slight increase in tissue between acini Parathyroids (3): Large and normal Heart Muscle: Well stained and normal; striations clear Voluntary Muscle (cross section): Normal Kidney: Glomeruli congested; tubules full of detritus; epithelium partly desquamated Intestine: Normal, pale stain Lung: Well stained; marked congestion Spleen: Normal except for many large areas of dark degenerated red cells Uterus and Tube: Normal and well stained
3	Rabbit: weight, 2.198 kg.; twice lethal dose, 1.1 c.c., diphtheria toxin followed by subcutaneous injections of morphin sulphate at successive intervals, as follows: 0 hr. 13 min., 30 mg.; 3 hr. 50 min., 20 mg.; 2 hr. 25 min., 40 mg.; 2 hr. 24 min., 40 mg.; 3 hr. 48 min., 40 mg.; 2 hr. 10 min., 40 mg.; 3 hr. 6 min., 20 mg.; total morphin, 230 mg.; died 22 minutes after last morphin injection; 18 hr. 18 min. after diphtheria toxin	Nearly all cells hyperchromatic and active	Nearly all cells hyperchromatic and active	Slight loss of cytoplasm and vacuolation in some cells	Cortex shows no loss of cytoplasm or vacuolation (medulla missing)	
4	Rabbit: weight, 2.658 kg.; twice lethal dose, 1.3 c.c., diphtheria toxin followed by subcutaneous injections of morphin sulphate at successive intervals, as follows: 0 hr. 26 min., 30 mg.; 3 hr. 43 min., 20 mg.; 2 hr. 30 min., 40 mg.; 2 hr. 10 min., 40 mg.; 4 hr. 9 min., 60 mg.; 1 hr. 56 min., 40 mg.; total morphin, 250 mg.; died 55 min after last morphin injection; 15 hr. 49 min. after diphtheria toxin	Nearly all cells hyperchromatic and active	Nearly all cells hyperchromatic and active; some fatigued	No loss of cytoplasm or vacuolation; well stained, nuclei central	Cortex shows no loss of cytoplasm or vacuolation (medulla missing)	
5	Rabbit: weight, 2.153 kg.; twice lethal dose, 1.1 c.c., diphtheria toxin followed by subcutaneous injection of morphin sulphate at successive intervals, as follows: 0 hr. 18 min., 30 mg.; 3 hr. 49 min., 40 mg.; 2 hr. 30 min., 40 mg.; 6 hr. 9 min., 40 mg.; 2 hr. 16 min., 40 mg.; total morphin, 190 mg.; died 50 minutes after last morphin injection; 15 hr. 56 min. after diphtheria toxin	Some hyperchromatic cells; nearly all active	Many hyperchromatic and active cells; some fatigued and exhausted	Slight loss of cytoplasm and small vacuoles in many cells; outlines and nuclei well stained		

* Experiments and histologic examinations by Ira A. B. Austin and E. W. Hitchings.

after last morphin injection; 15 hr. 58 min. after diphtheria toxin

* Experiments and histologic examinations by Drs. J. B. Austin and F. W. Hitchings.

TABLE 6.—*Histologic Effects of Diphtheria Toxin in Animals Under Ether and Under Nitrous Oxid Anesthesia.**

Exper.	Experimental Data	Cerebrum	Cerebellum	Liver	Suprarenals
1	Ether: Dog, weight, 6.800 kg.; when anesthesia complete, 5 c.c. diphtheria toxin intravenously; kept under anesthesia 4 hours and killed immediately	Some hyperchromatic cells; nearly all active	Many hyperchromatic and active cells; a few fatigued and an occasional exhausted cell	.....	Slight loss of cytoplasm and vacuolation in outer third of cortex; rest of cortex cells normal and full of cytoplasm; medulla normal
2	Ether: Dog, weight, 11.700 kg.; conditions as in Experiment 1	An occasional hyperchromatic and active cell; nearly all cells fatigued; some exhausted	No hyperchromatic cells; nearly all active; a few fatigued cells and an occasional exhausted cell	Slight loss of cytoplasm in some cells; no vacuolation	No loss of cytoplasm or vacuolation in cortex; medulla normal
3	Ether: Dog, weight, 7.300 kg.; conditions as in Experiment 1	No hyperchromatic cells; nearly all active; some fatigued; a few exhausted	No hyperchromatic cells; a few active; nearly all fatigued; an occasional exhausted cell	Slight loss of cytoplasm in cells of periphery of lobules; no vacuolation; majority of cells normal; nuclei deeply stained, slightly eccentric in cells which have lost cytoplasm	A slight loss of cytoplasm in a few outer cells of cortex; no large vacuoles; medulla normal
4	Ether: Dog, weight, 5.400 kg.; conditions as in Experiment 1	An occasional hyperchromatic and active cell; nearly all fatigued; some exhausted	No hyperchromatic cells; nearly all active; a few fatigued; an occasional exhausted cell	Slight loss of cytoplasm in some cells; no vacuolation	No loss of cytoplasm or vacuolation in cortex; medulla normal
5	Nitrous Oxid: Dog, weight, 6.452 kg.; conditions as in Experiments 1-4, except for anesthetic	Many active and some hyperchromatic cells; a few fatigued and exhausted	All Purkinje cells hyperchromatic	.....	Slight loss of cytoplasm in outer half of cortex; medulla normal

* Experiments and histologic examinations by Drs. J. B. Austin and F. W. Hitchings.

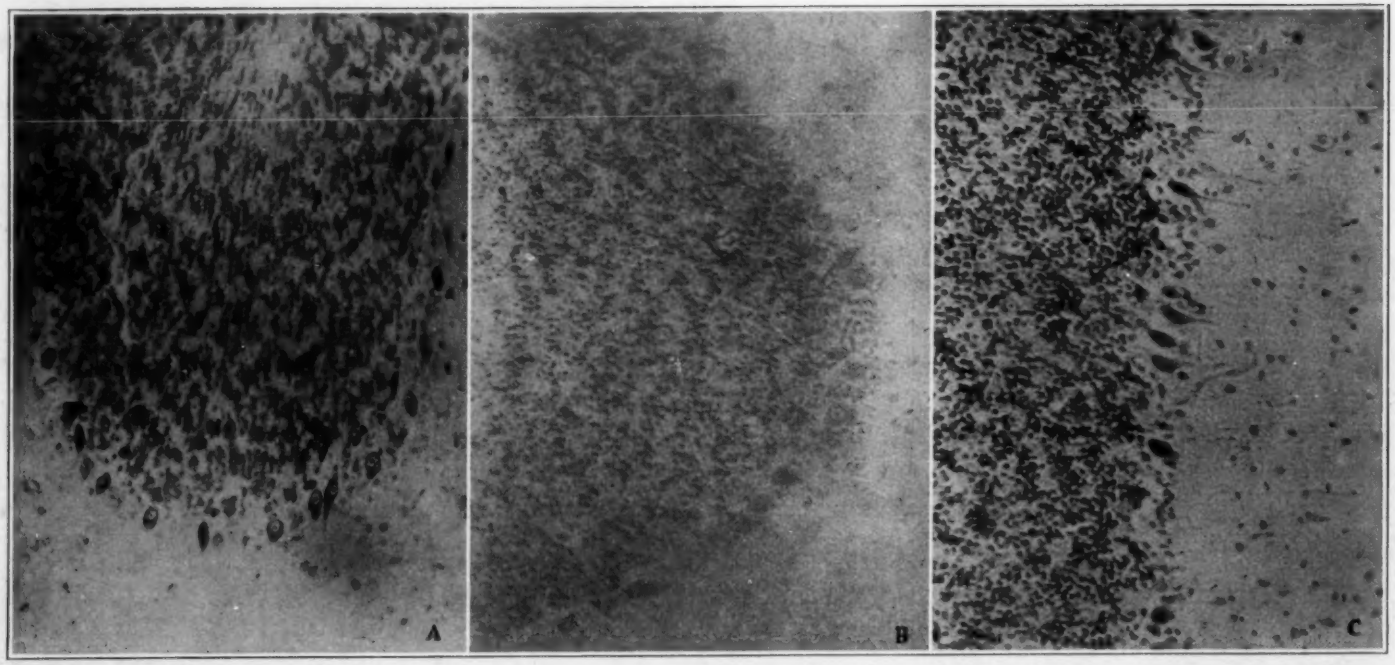

Fig. 5.—Comparative effects on the brain cells of diphtheria toxin alone and in the presence of morphin; *A*, section of the cerebellum of a normal rabbit; *B*, section of the cerebellum of a rabbit killed four hours after the injection of diphtheria toxin; *C*, section of the cerebellum of a rabbit killed four hours after the injection of diphtheria toxin administered after a massive dose of morphin (reduced from photomicrographs × 310).

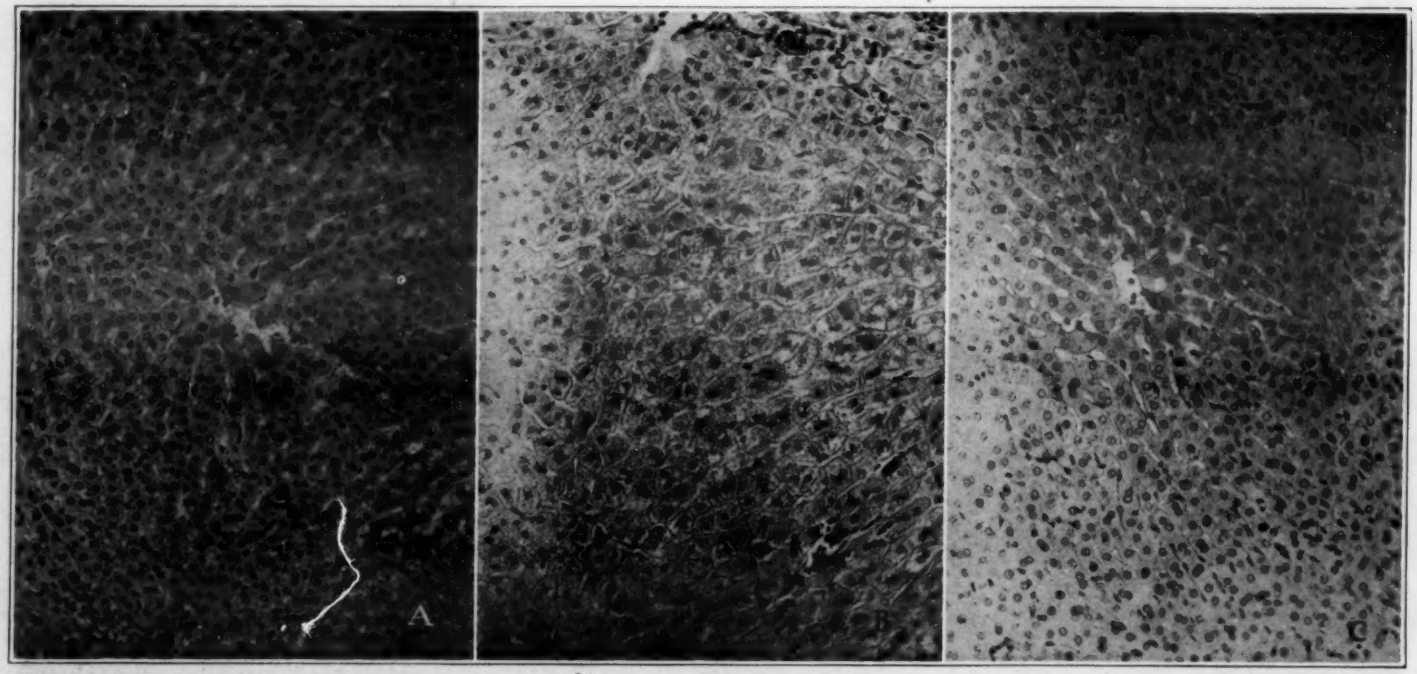

Fig. 6.—Comparative effects on the liver of diphtheria toxin and in the presence of morphin; *A*, section of the liver of a normal rabbit; *B*, section of the liver of a rabbit killed four hours after the injection of diphtheria toxin; *C*, section of the liver of a rabbit killed four hours after the injection of diphtheria toxin administered after a massive dose of morphin (reduced from photomicrographs × 310).

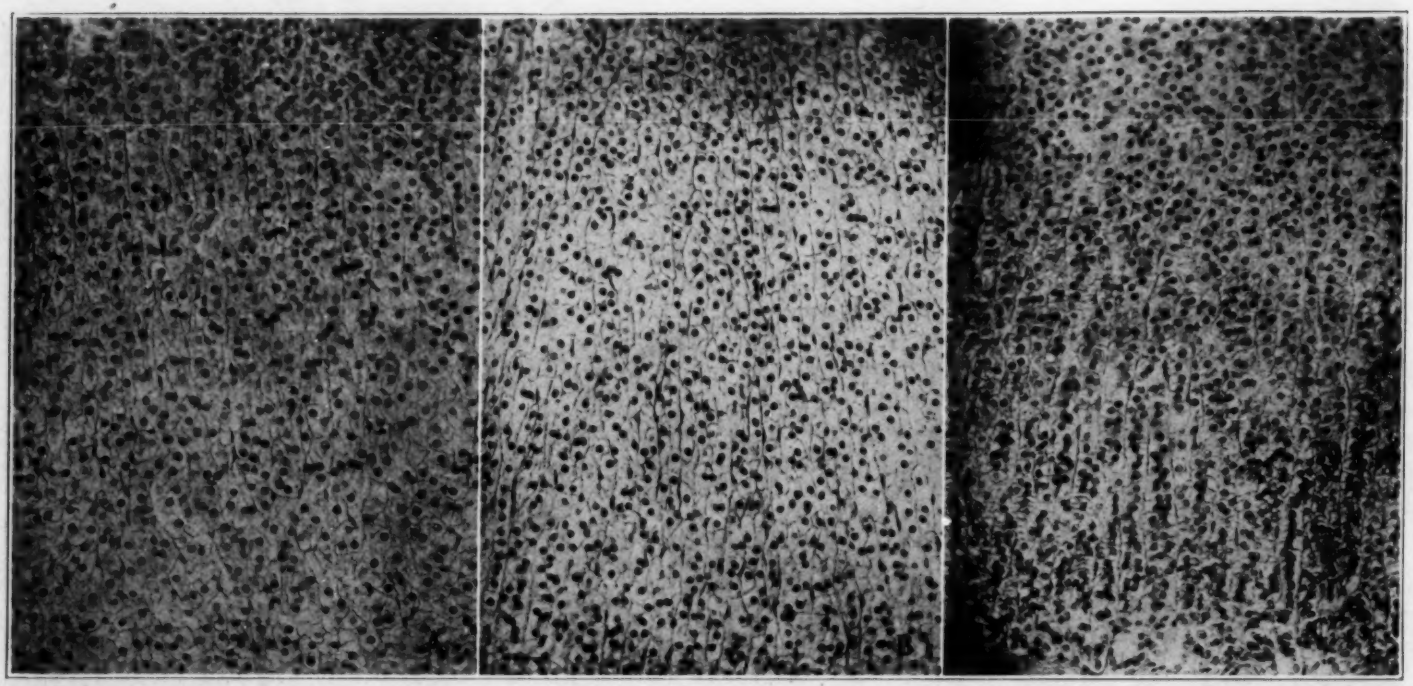

Fig. 7.—Comparative effects on the suprarenals of diphtheria toxin alone and in the presence of morphin; *A*, section of the suprarenal of a normal rabbit; *B*, section of the suprarenal of a rabbit killed four hours after the injection of diphtheria toxin; *C*, section of the suprarenal of a rabbit killed four hours after the injection of diphtheria toxin administered after a massive dose of morphin (reduced from photomicrographs × 310).

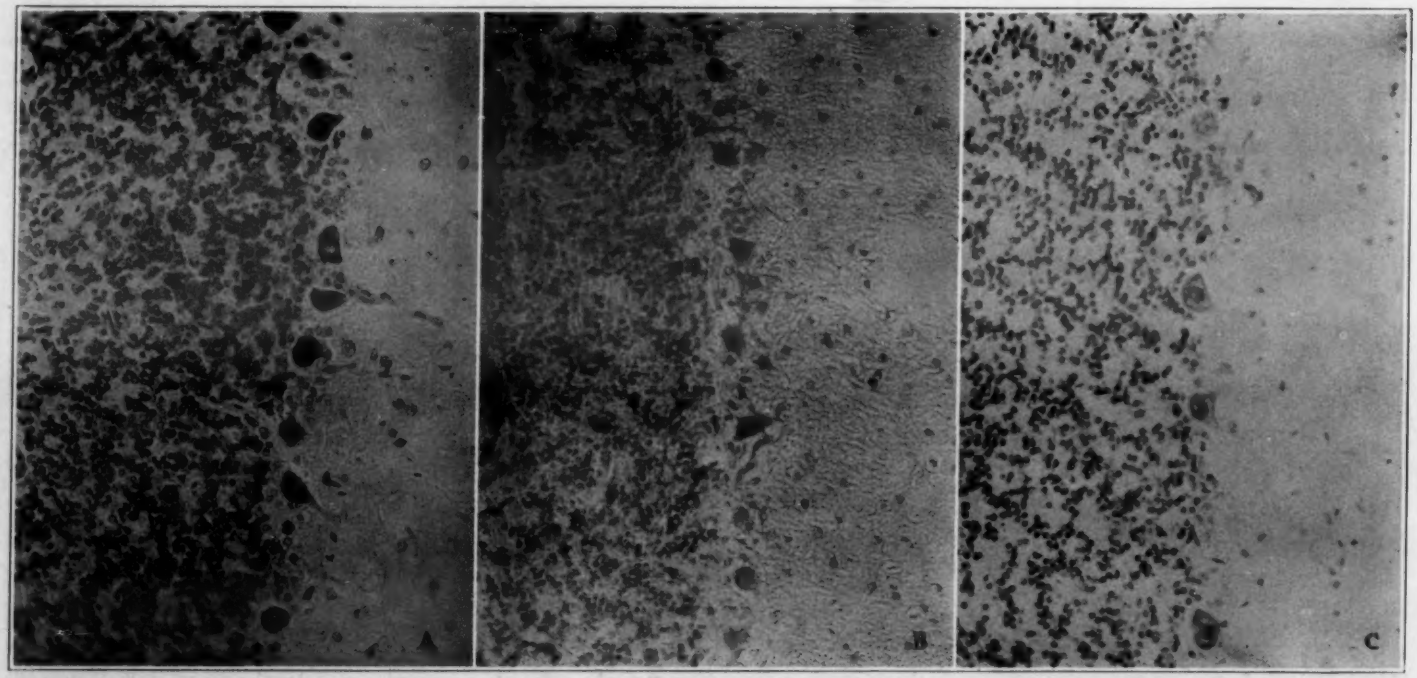

Fig. 8.—Comparative effects on the brain cells of diphtheria toxin alone and in the presence of ether anesthesia; *A*, section of the cerebellum of a normal dog; *B*, section of the cerebellum of a dog, killed four hours after the injection of diphtheria toxin; *C*, section of the cerebellum of a dog which had been kept under continuous ether anesthesia for four hours after the injection of diphtheria toxin (reduced from photomicrographs × 310).

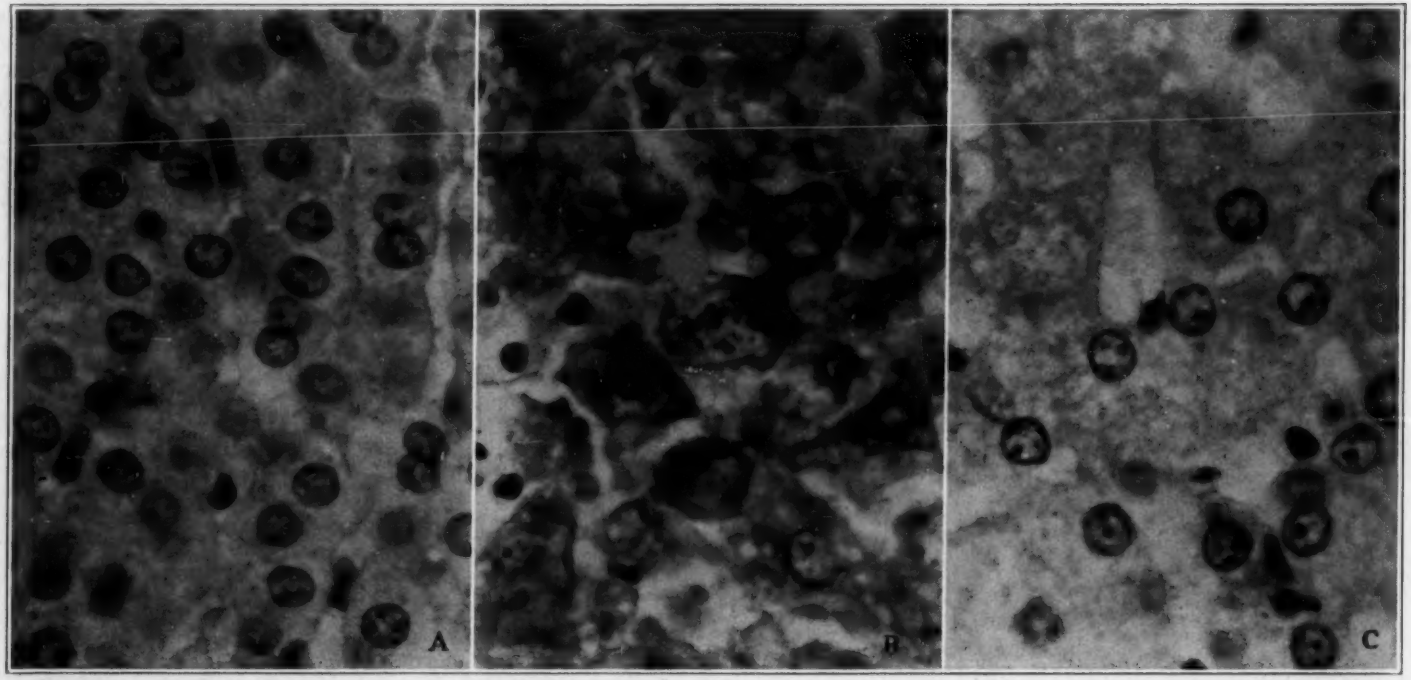

Fig. 9.—Comparative effects on the liver of diphtheria toxin alone and in the presence of ether anesthesia; *A*, section of the liver of a normal dog; *B*, section of the liver of a dog, killed four hours after injection of diphtheria toxin, *C*, section of the liver of a dog which had been kept under continuous ether anesthesia for four hours after the injection of diphtheria toxin (reduced from photomicrographs × 1,640).

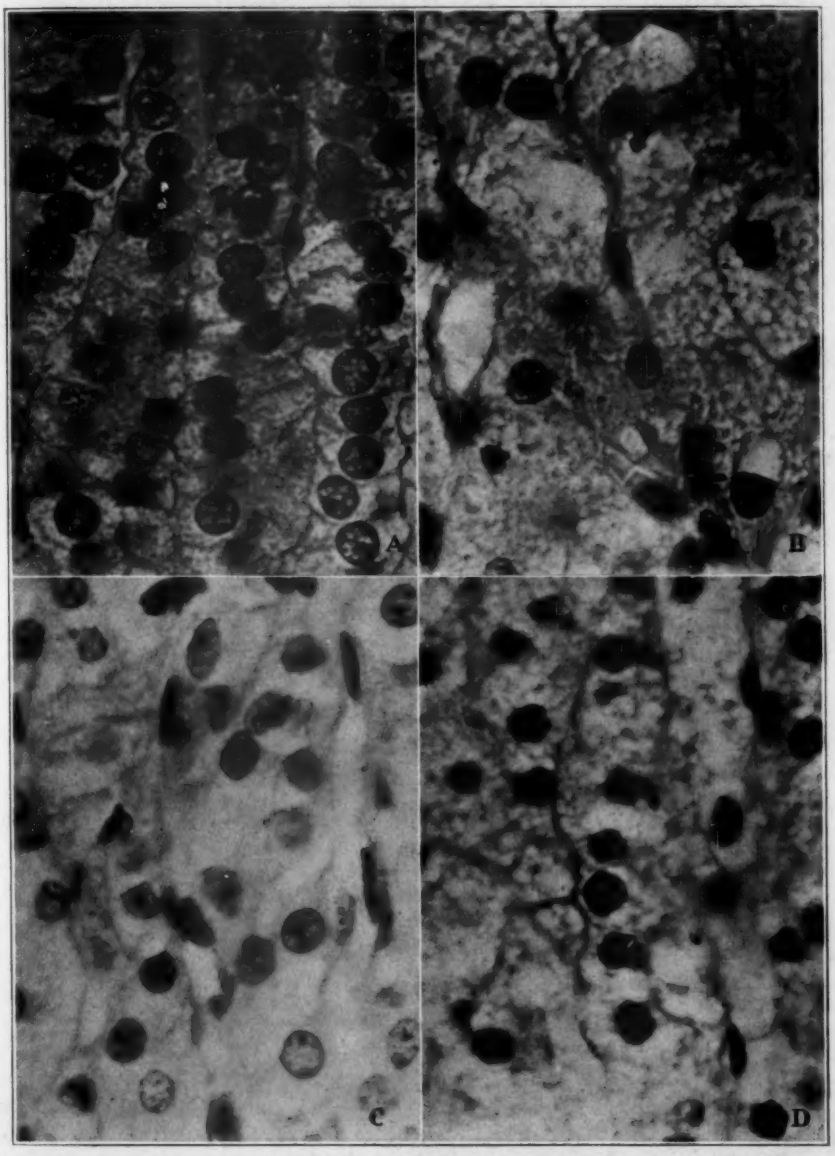

Fig. 10.—Comparative effects on the suprarenals of diphtheria toxin alone; in the presence of ether anesthesia, and in the presence of nitrous oxid anesthesia; *A*, section of suprarenal of a normal dog; *B*, section of suprarenal of a dog four hours after the injection of diphtheria toxin; *C* and *D*, sections of the suprarenals of dogs which had been kept under continuous anesthesia for four hours after the injection of diphtheria toxin (*C*, ether, *D*, nitrous oxid) (reduced from photomicrographs × 1,640).

SUMMARY OF HISTOLOGIC STUDIES

1. Septicemia is uniformly marked by histologic changes in the brain, the liver and the suprarenals.

2. The first histologic effect of the injection of a toxin was to increase the activity of the brain cells, as is indicated by an increased hyperchromatism. As the period between the injection of the toxin and the death of the animal was increased, there occurred a progressively increasing disintegration of the brain cells through the stages of fatigue to exhaustion.

3. The histologic changes in the suprarenals appear only in the cortex.

4. When the administration of a toxin was preceded by a massive dose of morphin or was followed by frequent repeated doses, the histologic changes were markedly diminished.

5. Continuous ether or nitrous oxid anesthesia diminished the histologic changes produced by a toxin.

6. In one experiment, the administration of a toxin to a decapitated animal prevented any histologic alteration of the suprarenals.

B. PHYSICOCHEMICAL AND FUNCTIONAL STUDIES

I. The Effect of Septicemia on the Suprarenal Output

Eight tests of the effect of the injection of bacterial toxins on the suprarenal output were made in our laboratory by Dr. F. W. Hitchings, with the uniformly positive results shown in Table 7 (Fig. 11).

In striking contrast are the results of two experiments in which the toxin was injected in morphinized animals, in each of which the test for epinephrin was negative (Table 8, Fig. 12).

II. Effect of Septicemia on the Chemical Content of Certain Tissues

The glands and tissues from eight cats which were subjects of a pyogenic infection, together with the glands and tissues from the same number of normal cats were sent to Parke, Davis & Co. for assay.

The results of these assays as given in Table 9 show that in the infected animals, as compared with the normal animals, (1) the iodin content of the thyroid gland was increased; (2) the epinephrin content and the epinephrin activity were decreased; (3) the glycogen content of the liver and of voluntary muscle was decreased, and (4) the pituitary activity was decreased.

TABLE 7.—*Effect of Injection of Bacterial Toxins on the Suprarenal Output (Cannon Test)**

Experiment	Animal and Anesthetic	Epinephrin Test 1 (Control) Before Injection	Toxin	Epinephrin Test 2 After Injection	Epinephrin Test 3 Second Test of Sample Used in Test 2
1	Cat; ether	Negative	Gonorrheal phylacogen, 1.5 c.c.	7 minutes after injection, positive	
2	Cat; ether	Negative	Mixed infection phylacogen, 2 c.c.	10 minutes after 2d injection, slight positive reaction	
3	Rabbit; ether	Negative	Saline suspension of B. typhosus, 2 c.c.	8 minutes after injection, positive	Same sample 27 min. later, negative
4	Cat; ether	Negative	Gonococcus endotoxin, 1 c.c.	5 minutes after injection, positive	Same sample 20 min. later, negative
5	Dog; ether	Negative	Gonorrheal phylacogen, 2 c.c.	5 minutes after injection, positive	Same sample 20 min. later, negative
6	Dog; ether	Negative	Mixed infection phylacogen, 2 c.c.	5 minutes after injection, positive	Same sample 20 min. later, negative
7	Dog; ether	Negative	Mixed infection phylacogen	5 minutes after injection, positive	Same sample 18 min. later, positive; 30 min. later, negative
8	Cat; ether	Negative	Tetanus toxin, 2 c.c.; 15 min. later, 10 c.c. toxin	5 minutes after 1st injection, delayed reaction; 5 min. after 2d injection, marked reaction	Same sample 20 min. later, negative

* Experiments by Dr. F. W. Hitchings.

TABLE 8.—*Effect of Injection of Bacterial Toxin on the Suprarenal Output in a Morphinized Animal (Cannon Test)**

Experiment	Animal and Anesthetic	Epinephrin Test 1 Before Injection	Toxin	Epinephrin Test 2 After Injection	Epinephrin Test 3 After Oxidation of Sample
1	Dog; etherized after morphin gr. 1; 30 min. after injection of toxin, 2d dose of morphin gr. 2.25	Negative	Diphtheria toxin, 2.5 c.c.; 15 min. after 2d dose morphin, 5 c.c. toxin	5 minutes after injection, positive; 5 min. after 2d injection, negative	Same sample 25 min. later, negative
2	Dog; etherized after morphin gr. 1	Negative	Gonococcus endotoxin, 7 c.c.	8 minutes after injection, negative	

* Experiments by Dr. F. W. Hitchings.

TABLE 9.—*The Effect of Septicemia on the Chemical Content of Certain Organs and Tissues**

	Thyroid: Iodin Content, per Cent.	Suprarenals		Liver: Glycogen Content, per Cent.	Muscle: Glycogen Content, per Cent.	Hypophysis: Pituitrin Activity, per Cent.
		Epinephrin Content, per Cent.	Epinephrin Activity, per Cent.			
Normal cats.....	0.0156	0.1	5 (of standard)	0.508	0.56	25 (of standard)
Infected cats.....	0.0225	0.037	2 (of standard)	0.208	Trace	16⅔ (of standard)

* Experiments by A. F. Rowland; assays by Parke, Davis & Co.

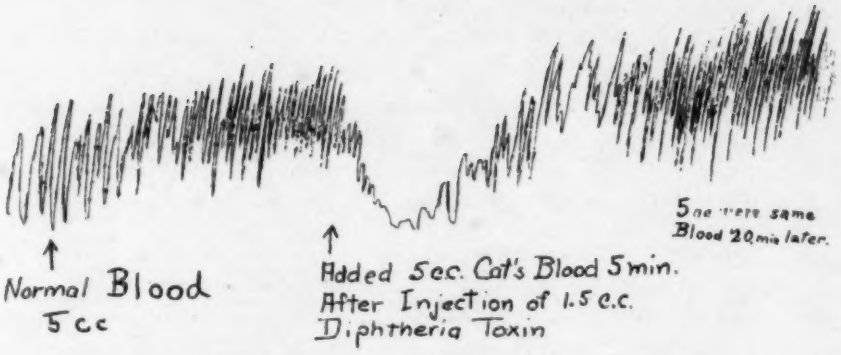

Fig. 11.—Effect of the injection of diphtheria toxin on the suprarenal output (Cannon test).

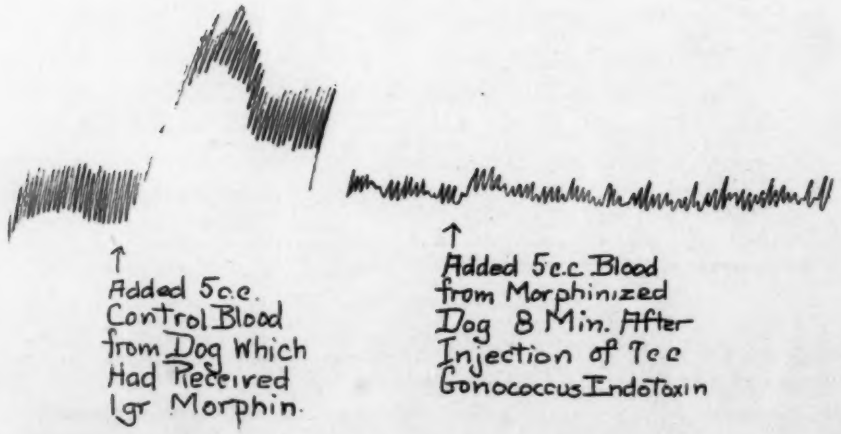

Fig. 12.—Effect on the suprarenal output of the injection of gonococcus toxin in a morphinized dog.

III. The Effect of Bacterial Toxins on the H-Ion Concentration and Reserve Alkalinity of the Blood

In six experiments in which the H-ion concentration of the blood was tested at varying intervals after the injection of tetanus or diphtheria toxin, it was either unchanged or decreased in every case but one (Experiment 3, Table 10).

Table 10.—*Effect of Bacterial Toxins on the H-Ion Concentration of the Blood* *

Experiment	Experimental Data	Source of Blood	p_H Before Injection	p_H After Injection
1	Dog under ether; blood taken before and immediately after injection of tetanus toxin, 2 c.c.	Vena cava Liver	7.02 7.04	7.01, 7.02 7.04, 7.08
2	Dog under ether; blood taken before and 6 (liver) to 8 (vena cava) minutes after injection of tetanus toxin, 14 c.c.	Liver Vena cava	7.24, 7.20 7.24, 7.28	7.31, 7.30 7.28, 7.21
3	Dog under ether (weight, 11.255 kg.); blood taken before and 7 (suprarenal), 10 (vena cava), and 12 (liver) minutes after injection of tetanus toxin, 25 c.c.	Suprarenal Vena cava Liver	7.31, 7.42 7.36, 7.24 7.22	7.24, 7.24 7.15 7.41
4	Rabbit; blood taken before and immediately after injection of diphtheria toxin, 0.5 c.c.	Femoral	7.324	7.48, 7.51
5	Rabbit; blood taken before and 2 and 37 minutes after injection of diphtheria toxin, 0.6 c.c.	Ear	7.41, 7.43	2 min., 7.44, 7.41; 37 min., 7.51, 7.50
6	Rabbit; blood taken before and 20, 90 and 115 minutes after injection of diphtheria toxin, 0.6 c.c.	Ear	7.70, 7.68	20 min., 7.66, 7.70; 90 min., 7.67, 7.66; 115 min., 7.70

* Experiments by Dr. M. L. Menten.

Table 11.—*Effect of Bacterial Toxin in the Presence of Morphin on the H-Ion Concentration of the Blood* *

Experiment	Experimental Data	p_H Before Morphin	p_H Before Injection of Toxin	p_H After Injection of Toxin
1	Rabbit (weight, 2.140 kg.); diphtheria toxin, 0.5 c.c., injected 1 hr. 32 min. after intravenous injection of 4 c.c. of 1% solution morphin sulphate; second dose morphin (same amount), 25 min. later; blood taken (1) before and (2) 10 and (3) 45 min. after first morphin injection (4) immediately and (5) 40 min. after injection of diphtheria toxin (15 min. after second dose morphin)	(1) 7.59, 7.59	(2) 7.35, 7.35 (3) 7.33, 7.35	(4) 7.59, 7.64 (5) 7.09, 7.125
2	Rabbit: Diphtheria toxin, 0.6 c.c., injected 25 min. after intravenous injection of morphin sulphate, gr. 1; blood taken 20 min. after injection of morphin, 5 min. after injection of diphtheria toxin	.....	7.41	7.00, 7.10

* Experiments by Dr. M. L. Menten.

In two experiments in which the injection of the toxin was preceded by the injection of morphin, the H-ion concentration of the blood was increased (Table 11). In the first experiment of this group, time was allowed for the H-ion content of the blood to become stabilized after the injection of the morphin, before the toxin was injected. As will be noted, immediately after the injection of toxin the H-ion concentration corresponded to the normal concentration before the morphin

was given, the increase occurring later. In Table 10, the length of time after the toxin was injected apparently made no difference.

In one other experiment, tetanus toxin was injected in a dog after the spinal cord had been severel. H-ion estimations gave the following results: Forty minutes after the cord was severed, p_H, 7.43, 7.48; sixty-five minutes after, p_H, 7.46, 7.43. Eighty-nine minutes after the cord was severed, 22 c.c of tetanus toxin was injected. The results

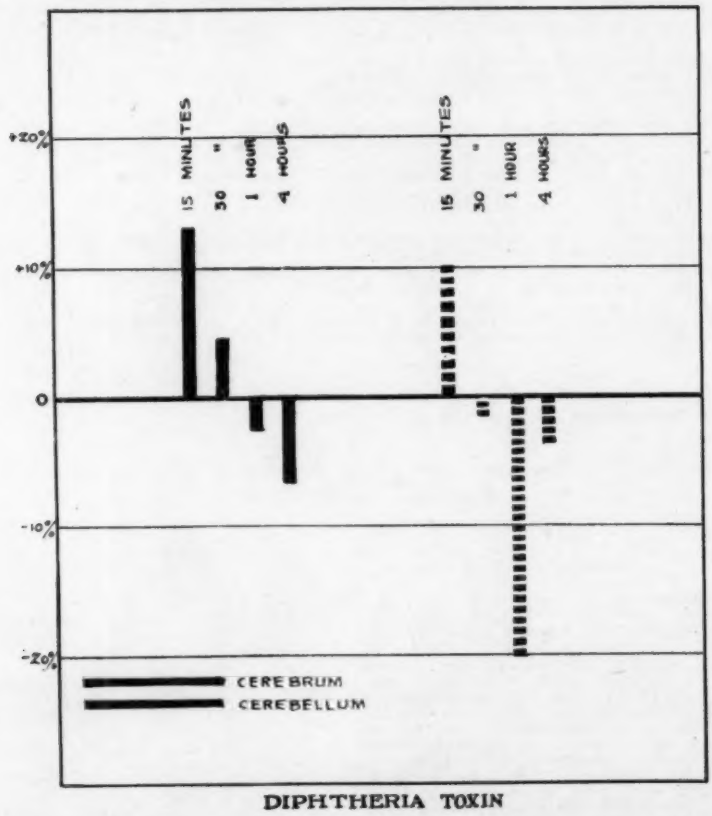

Fig. 13.—The incipient and later effects of the injection of diphtheria toxin on the electrical conductivity of the brain (percentile variations from the normal).

were: Six minutes after injection of toxin, p_H, 7.49; twenty minutes after, p_H, 7.46; one hour eleven minutes after, p_H, 7.45. A second dose of toxin, 20 c.c, was given one hour and fifteen minutes after the first injection. Eight minutes after, p_H was 7.40, 7.43.

It would appear that the H-ion concentration of the blood is not altered in the earlier periods after the injection of bacterial toxin but

that in the presence of morphin, possibly through some interference with the processes of neutralization, the H-ion concentration of the blood is markedly increased.

A measurement of the reserve alkalinity of the blood of a dog, made by Dr. W. B. Rogers with the Van Slyke method, showed a diminution in the carbon dioxid combining power from 42 c.c. per hundred cubic centimeters of plasma to 39 c.c., twenty-one hours after the injection of *Staphylococcus albus* into the peritoneal cavity.

IV. Electric Conductivity Measurements of the Effects of Bacterial Toxins

To various groups of rabbits twice the lethal dose of diphtheria toxin (Parke, Davis & Co.) was given intravenously, the animals being

Table 12.—*Progressive Effects of the Injection of Diphtheria Toxin upon the Electrical Conductivity of the Brain*

Date of Experiment	Period After Injection of Toxin	Number of Animals	Electric Conductivity of Cerebrum	Average Deviation, per Cent.	Percentile Deviation from Normal, per Cent.	Number of Animals	Electric Conductivity of Cerebellum	Average Deviation, per Cent.	Percentile Deviation from Normal, per Cent.
5/12–5/27/19	Normal V	6	00185	1.5		7	00137	3	
6/ 2–6/ 4/19	15 min.	2	00226	1.9	+22.0	3	00137	0.9	0
6/ 2–6/ 4/19	30 min.	3	00194	1.3	+ 4.8	3	00128	1.8	— 6.5
5/27–5/29/19	1 hour	3	00180	1.7	— 2.7	3	00109	0.5	—20.4
12/ 3/19–1/6/20	Normal XI	7	00172	2.4		8	00127	2.8	
12/15/19–1/2/20	15 min.	3	00189	1.2	+ 9.8	3	00154	1.7	+21.2
1/ 7/20	30 min.	2	00174	3.8	+ 4	2	00131	0	+ 3.1
1/3–2/19/19	Normal III	5	00192	1.6		5	00162	5.3	
2/8–2/18/19	4 hours	5	00179	2.7	— 6.7	6	00156	3.1	— 3.8

* Experiments by Helen R. Hosmer and Amy F. Rowland.

killed at intervals varying from five minutes to one hour after the dose was received. As will be seen from Table 12 and Figure 13, the early effect of the injection of diphtheria toxin is to increase the conductivity of the brain, the increase becoming progressively less until from thirty minutes to one hour after the injection, when it begins to decrease below the normal.

In another group of experiments, 5 grains of morphin was given hypodermically in two doses, one hour apart; twice the lethal dose of diphtheria toxin being given intravenously fifteen minutes after the second dose of morphin. The animals were killed four hours after the second dose of morphin was received. Electric conductivity measurements of the brain and the liver as given in Table 13 and illustrated in Figure 14 show that the changes produced by the administration of diphtheria toxin in the presence of morphin are markedly less than when the diphtheria toxin alone is given.

TABLE 13.—*Comparison of the Effects of Diphtheria Toxin Alone and of Diphtheria Toxin in the Presence of Morphin on the Electrical Conductivity of the Brain and the Liver*

Date of Experiment Group	Stimulus	Number of Animals	Electric Conductivity of Cerebrum	Average Deviation, per Cent.	Percentile Deviation from Normal	Number of Animals	Electric Conductivity of Cerebellum	Average Deviation, per Cent.	Percentile Deviation from Normal	Number of Animals	Electric Conductivity of Liver	Average Deviation, per Cent	Percentile Deviation from Normal
12/14-12/21/18	Normal III.....	6	00192	1.6		6	00162	5.3		3	00074	2.2	
2/ 8-12/18/19	Diphtheria toxin.....	5	00179	2.7	—6.7	6	00156	3.1	—3.7	4	00069	3.0	— 6.7
2/ 6- 2/13/19	Morphin.....	6	00185	4.6	—3.6	6	00148	4.1	—8.6	6	00065	6.9	—12.2
2/ 6- 2/18/19	Diphtheria toxin and morphin.....	6	00187	2.6	—2.6	6	00164	3.2	+1.2	6	00075	4.2	+ 1.4

* Experiments by Helen R. Hosmer and Amy F. Rowland.

V. Thermo-electric Studies of Temperature Variations in the Brain and the Liver in the Presence of Bacterial Toxins

Direct measurements of the temperature of the brain and the liver by means of thermocouples were made continuously for hours after the injection in two rabbits of twice the lethal dose of diphtheria toxin. As will be seen by Figures 15 and 16, the temperature of the liver was

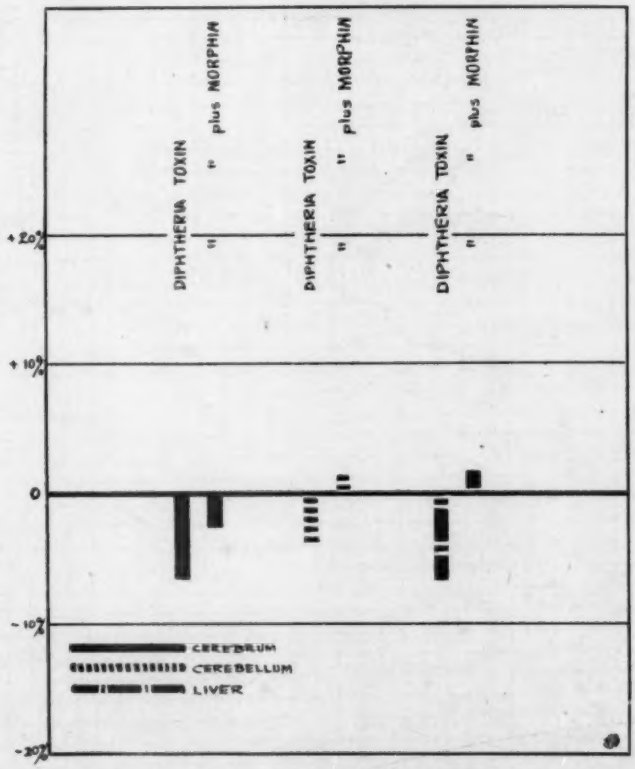

Fig. 14.—Comparative effects of the injection of diphtheria toxin alone and in the presence of morphin, on the electrical conductivity of the brain and the liver (percentile variations from the normal).

not affected. The temperature of the brain, however, showed marked variations, which bear a rough resemblance to those which are produced by successive doses of epinephrin.

One of the animals (Fig. 16) was kept alive for twenty-four hours, and the thermocouples were again inserted and ether administered. The abrupt fall in the temperature, to death within ten minutes, indicates an advanced state of exhaustion of the brain.

C. CLINICAL EVIDENCE

The clinical phenomena of acute and of chronic infection are matters of daily observation. The temperature variations, psychic disturbances and acute or progressive signs of exhaustion, each in relation to the severity or protraction of the septicemia, need no detailed description.

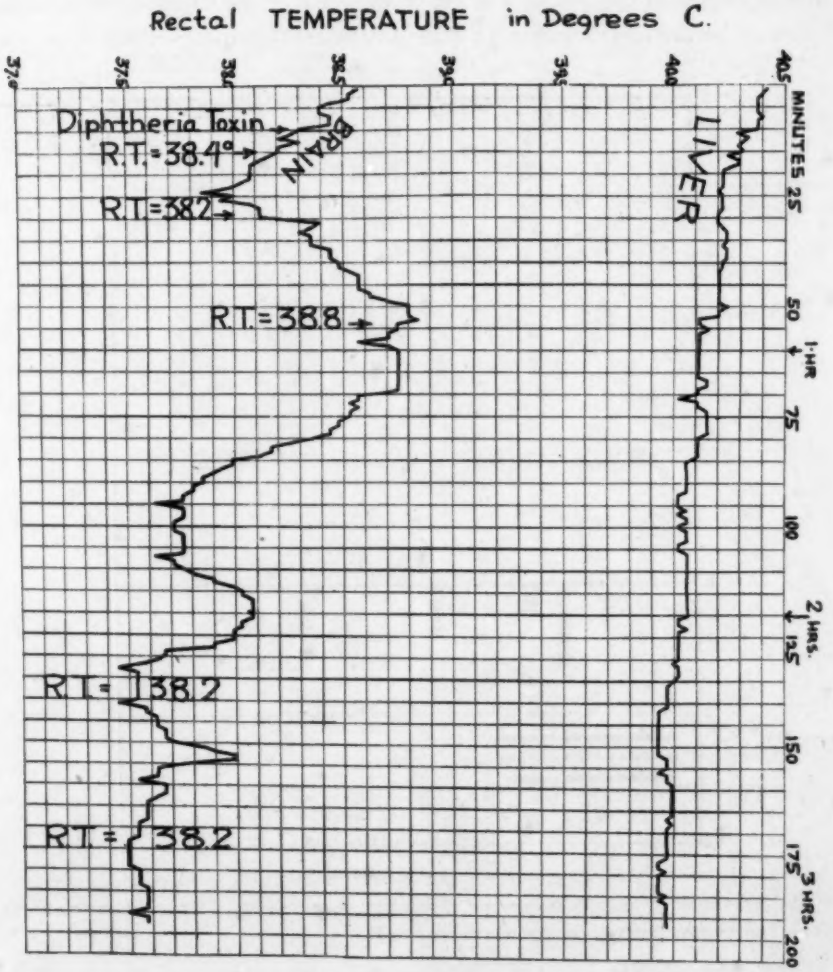

Fig. 15.—Comparative effects of the injection of diphtheria toxin on the temperature of the brain and the liver.

One phase only of our clinical observations should be recorded here, since it is correlated with the comparative effects on the brain cells of the injection of diphtheria toxin, with and without morphin.

Five animals (rabbits) were given a lethal dose of morphin; and to five others, 2 grains of morphin in divided doses was given after the

injection of a lethal dose of the toxin. The length of life of the animals in the two groups and the progressive changes in temperature were noted.

The average duration of life of the animals which received the morphin was fifteen hours and three minutes; of the others, twelve hours and fifty-two minutes.

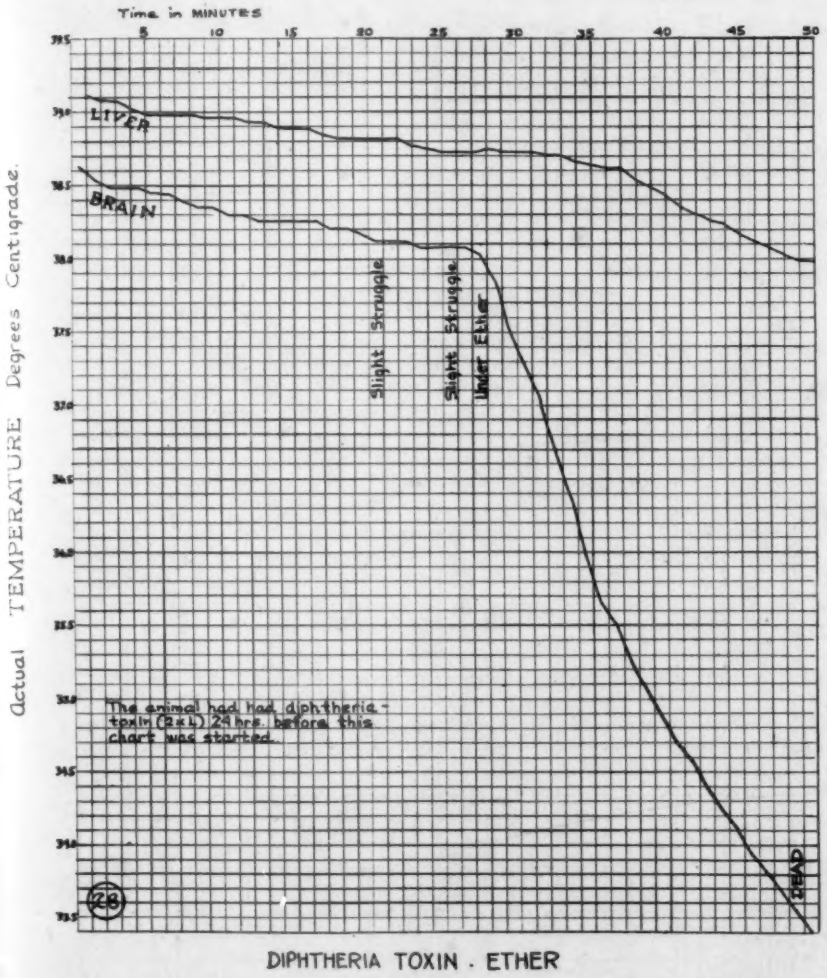

Fig. 16.—Effect of the administration of ether on the temperature of the brain and the liver twenty-four hours after the injection of diphtheria toxin. The rapid decline in the temperature of the brain and the almost complete lack of response in the temperature of the liver may be noted.

Of special significance is the comparison of the variations in temperature, which are graphically shown in Figure 17. These temperature variations are closely in accord with the histologic changes in the brain.

GENERAL SUMMARY

1. The effects of septicemia have been studied (*a*) by histologic observations; (*b*) by measurements of the H-ion concentration and of the alkali reserve of the blood; (*c*) by estimations of the iodin content of the thyroid gland, of the epinephrin content of the suprarenals and

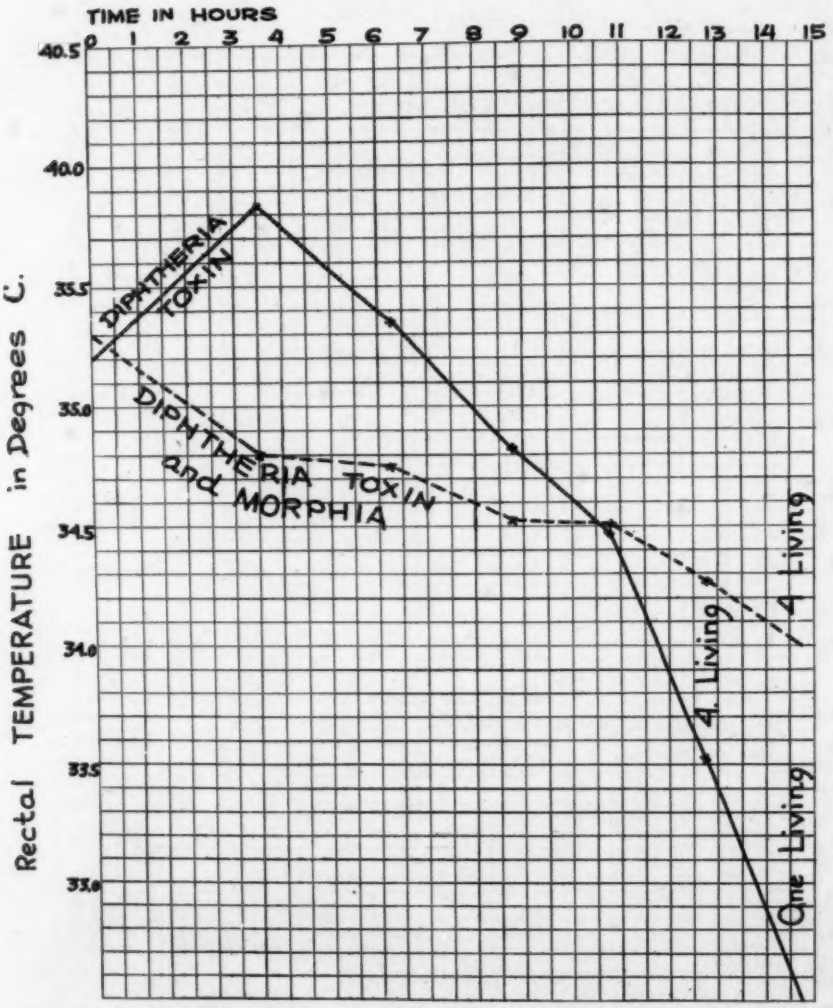

Fig. 17.—Comparison of the progressive temperature changes (rectal) after the injection of diphtheria toxin in a normal and in a morphinized rabbit.

the epinephrin activity, of the pituitrin activity, of the glycogen content of the liver and of voluntary muscle; (*d*) by measurements of the electric conductivity of the brain and the liver; (*e*) by direct measurements of the temperature of the brain and the liver, and (*f*) by clinical observations.

2. All these lines of investigation indicate that changes in the central nervous system are the primary cause of the cycle of phenomena which mark the progress of the exhaustion which is the end-result.

3. The experimental evidence indicates that the liver and the suprarenals are associated with the brain in the production of the phenomena which are initiated by the changes in the brain.

4. The limitation of the changes produced in normal animals by an infection, by the presence of agents which depress the activity of the central nervous system, strongly supports the conclusion that the brain is the primary factor in the response to infection.

THE VALUE OF SGAMBATI'S REACTION FOR ACUTE PERITONITIS*

HANS DEUTSCH, M.D., AND EVARTS A. GRAHAM, M.D.
ST. LOUIS

In 1920, Sgambati [1] described a reaction in the urine based on the presence of what he called chromogenic substances specific in cases of acute peritonitis. Since then, this test has been referred to in Italian literature as Sgambati's test, and great importance has been attached to it by Solieri [2] and others who have used it, not only diagnostically but also in prognosis of their cases in which operation has been performed. They all agree that the test indicates not only the gravity of the infection but also the virulence of the organism involved. Solieri states that he found the test useful in determining the time of operative interference in threatening perforating typhoid ulcers of the intestine.

The test was originally described thus:

Two or three c.c. of concentrated nitric acid is added to 8 or 10 c.c. of urine in a test tube in such a manner as to form a contact zone (i. e., without mixing the liquids). Above the zone of contact, which is reddish brown (obtained in any urine), a blue-gray color develops in case the reaction is positive. After standing, this color diffuses throughout the urine, and after several hours without shaking a ruby red color can be extracted with chloroform. According to Sgambati, the blue-gray as well as the ruby red are oxidation products of chromogens pathognomonic of peritonitis, and their intensity varies directly with the gravity of the condition as well as the virulence of the infection. He was unable to state anything further about the exact nature of the substance. Solieri, from his experience, believes that the resistance to peritoneal infection is developed by the peritoneal cells themselves rather than by antibodies formed in the blood, and therefore he looks on the chromogens described by Sgambati as furnishing a direct index to the activity of the peritoneum.

In the present investigation to determine the usefulness of this test, it was found that positive reactions occurred both with and in the absence of peritonitis. In the following tables, the cases are arranged according to the presence or absence of peritonitis.

---

*From the Department of Surgery, Washington University School of Medicine.

1. Sgambati, O.: Policlinico (sez. prat.) **27**:267 (March 1) 1920.
2. Solieri, S.: Policlinico (sez. prat.) **29**:651 (March 15) 1922.

TABLE 1.—*Cases with Definite Peritonitis*

Case	Peritonitis	Sgambati's Test	Remarks
1. Inguinal hernia, strangulated	General	Strongly +	Peritonitis confirmed at necropsy
2. Appendicitis, acute....	General, present at operation	Strongly +	Confirmed at necropsy, streptococcus culture
3. Appendicitis, acute, ruptured	Local	Strongly +	Patient recovered; Bacillus coli culture
4. Carcinoma of stomach	General	Strongly +	Confirmed at necropsy
5. Appendicitis, acute, ruptured	Local	Definitely +	Patient recovered; Bacillus coli culture
6. Intestinal obstruction, fecal fistula	Local	Strongly +	Negligible amount of pus around fistula at necropsy; death due to intestinal obstruction and not to peritonitis
7. Rupture of intestine...	General	Definitely +, but not strongly	Confirmed at necropsy

TABLE 2.—*Cases with Signs of Inflammation but No Pus*

Case	Peritonitis	Sgambati's Test	Remarks
8. Appendicitis, acute....	Some free fluid at operation	Definitely +	Uneventful recovery
9. Appendicitis, acute....	Appendix very red	Definitely +	Uneventful recovery
10. Intestinal obstruction	Small amount of free fluid	Strongly +	Uneventful recovery

TABLE 3.—*Cases with Questionable Signs of Peritonitis*

Case	Peritonitis	Sgambati's Test	Remarks
11. Ulcer of stomach.....	Doubted	Definitely +	Recovered; no operative interference
12. Appendicitis, acute (?)	Local tenderness and rigidity	Negative (indican also negative)	Acute salpingitis found at operation
13. Typhoid fever.....	Slight rigidity, tenderness	Faintly +	

TABLE 4.—*Cases in Which No Peritonitis Was Found*

Case	Peritonitis	Sgambati's Test	Remarks
14. Inguinal hernia strangulated	No evidence at operation	Strongly + postoperative	Patient died 24 hours after operation
15. Carcinoma of stomach.....	No evidence at operation	Strongly + postoperative	No evidence found at necropsy
16. Tumor of splenic flexure of colon	No evidence at operation	Definitely + preoperative	Uneventful recovery
17. Typhoid fever.....	Clinically questionable, constant hiccup	Strongly +	No evidence found at necropsy; death due to intestinal hemorrhage
18. Myocarditis, chronic; cardiac decompensation	Ascites	Strongly +	No necropsy obtained; death due to cardiac condition
19. Cardiac decompensation.....	Ascites	Definitely +	Death due to cardiac condition
20. Postepileptic state.....	No abdominal symptoms	Definitely +	Patient under morphin constantly for 36 hours
21. Simple constipation.....	No symptoms	Definitely +	Student up doing daily duties
22. Carcinoma of the larynx.....	No symptoms	Definitely +	Sedatives; no bowel movement for 36 hours

From the results tabulated, it is evident that, by means of Sgambati's test, one could not tell the condition of the peritoneum. Comparing Cases 2 and 3, one being a *Streptococcus* and the other a *Bacillus coli* infection, both giving a strongly positive reaction, and Case 5, an identical infection with Case 3, on the other hand, giving a decidedly weaker reaction, it would be difficult to decide the virulence of the infection from the test. In most of the cases, the signs of peritonitis were either definitely present or absent, and Sgambati's test would not have influenced the treatment of the condition. In only one case (Case 12) in which the differentiation between acute appendicitis and acute salpingitis came up was Sgambati's test negative, and no peritonitis was found at operation, but an acutely inflamed right tube. Here, however, the test for indican was also negative, which seemed very striking, since indican was always present with a positive Sgambati test. In fact, the urines which gave a strongly positive reaction contained such a large quantity of indican that they turned black on exposure to air for several days. The reaction was easily obtained with larger amounts of indican regardless of the condition of the peritoneum, as evidenced in Table 4, but was either faint or absent with smaller amounts of indican. Marcialis [3] attributed the formation of the blue-gray color in the first part of Sgambati's test to the presence of indican and other putrefactive products, such as phenol; and he therefore disregards this part of the reaction, in contradistinction to the belief of Sgambati. The red, Marcialis argues, is due to oxidation products of chromogens found only in peritonitis, as Sgambati and his followers believe.

Results of this present investigation further showed that the red was associated with indican. The blue obtained in the first part of the reaction was extracted with chloroform, and after washing and gentle agitation with dilute nitric acid, the red developed and the blue disappeared. The same was true of the indigo blue obtained with Obermayer's reagent. Incidentally, it may be mentioned that the iodin in the urine of patients receiving iodids internally will be set free by nitric acid and give a color in chloroform which will make it impossible to see the color developed in Sgambati's reaction and may be mistaken for a positive reaction.

In the study of the chemistry of indigo, it was found that Rosin [4] isolated indigo red (indirubin, or indigo purpurin) from the urine as early as 1889, an indigo dye the chemistry of which was demonstrated

3. Marcialis, G.: Biochem. e terap. Sper. **9**:101, 1922.
4. Rosenbach, O.: Berl. klin. Wchnschr. **27**, 1889; **28**, 1890.

by Schunk [5] (1856) and Baeyer [6] (1879). Rosin [7] did this most extensive work to identify the red formed in Rosenbach's [4] test for red indol and skatol pigments, a test in which nitric acid is used as an oxidizing agent, differing from Sgambati's test only in that the acid is added drop by drop to boiling urine (which, by the way, hastens the reaction), rather than adding it to the cold. The presence of indigo red is of no more importance than the presence of indigo blue since both arise from the same source.

The red isolated in Sgambati's test [8] corresponds to indigo red in that it is soluble in chloroform, ether, benzol and alcohol, and in glacial acetic acid, from which it can be precipitated with sodium carbonate and water. It is more stabile to oxidizing agents than indigo blue, of which it is an isomer, but it is destroyed by an excess of nitric acid. From these facts and the conclusive evidence in Rosin's work, the following conclusions seemed justified:

CONCLUSIONS

1. Sgambati's reaction is not specific for peritonitis.
2. The red obtained by this reaction is indigo red, an oxidation product of indoxyl.
3. Its diagnostic importance is similar to that of indican.

---

5. Schunk, E.: Ber. d. deutsch. chem. Gesellsch. **12**:1220, 1879; Mem. Manchester Phil. Soc. 2d Series **14**:185-237, 1856.

6. Baeyer, A.: Ber. d. deutsch. chem. Gesellsch. **12**:475, 1879; **14**:1145, 1881.

7. Rosin, H.: Centralbl. f. lin. Med. **10**, No. 29, 1889.

8. In order to obtain results more quickly than stated by Sgambati, one may add the chloroform to the urine as soon as the blue develops and then, after gently agitating, allow it to stand from ten minutes to one-half hour. The color intensifies on further standing.

MULTIPLE BILATERAL TRAUMATIC PAROSTEAL BONE AND CALLUS FORMATIONS OF THE FEMURS AND LEFT INNOMINATE BONE*

REPORT OF CASE

EBEN J. CAREY, M.D.

CHICAGO

The development of parosteal bone within muscle following trauma has become an important and interesting surgical problem since the advent of the roentgen ray, which has made more certain the diagnosis of the condition, and the increasing incidence of injuries due to occupation. The intense interest in this condition resulted from the increasing demands made by accident insurance companies upon the surgeon for a more definite prognosis following injury to muscle and bone, because of the workmen's compensation law.

Josephson,[1] in 1874, made the first collection from the literature of fifty-eight cases of what he called muscular osteomas, and Cahier,[2] in 1904, gathered 133 cases. Schulz,[3] 1903, gathered 296 and, in 1912, Jones and Morgan[4] collected 339 cases. During the last decade the recorded cases have numbered in the thousands.

All the theories of traumatic bone formation in muscle include the factor of initial injury. In the vast majority of cases, there is but one severe injury caused by a blunt force, and of the 296 cases of ossification in muscle collected by Schulz not less than 232 gave a history of one severe contusion.

Opinions, however, vary among observers as to what takes place following the injury. This is inevitable because these parosteal bone masses have not been reproduced experimentally with any degree of constancy by Berthier,[5] and the sequence of events has not been followed in series from the beginning to the end of the process. The end-results of the parosteal bone formation have been studied, and a number of theories have been advanced concerning the process.

1. The hemic theory of Seydeler,[6] who held that the hemorrhagic blood organized was first transformed into cartilage and then into bone.

---

* From the Pathological Laboratory, Rush Medical College.

* Read before the Chicago Pathological Society, Jan. 8, 1923.

1. Josephson, A.: Deutsch. mil. Ztschr. **2**:156-161, 1874.
2. Cahier, L.: Rev. de chir. **29**:356-367, 1904.
3. Schulz, O.: Deutsch. mil. Ztschr. **36**:339-348, 1903.
4. Jones, Robert, and Morgan, David: Arch. Roentg. Rays **9**:245-249, 1905; ibid. **10**:99-100, 1906.
5. Berthier, A.: Arch. de méd. expér. et d'anat. path. **6**:601-620, 1894.
6. Seydeler, R.: Deutsch. mil. Ztschr. **8**:33-48, 1879.

2. The theory of aberrant sesamoid bones of Bard,[7] who held that under the stimulus of trauma such bones proliferate and assume considerable proportions.

3. The theory of detached periosteal flaps of Graf [8] and Berthier,[5] who consider these flaps or detachments of the periosteum as giving rise to the bone. Berthier, experimenting with rabbits, detached portions of the periosteum at the muscular insertions and then stimulated the muscles electrically. There was subsequently found in a few of

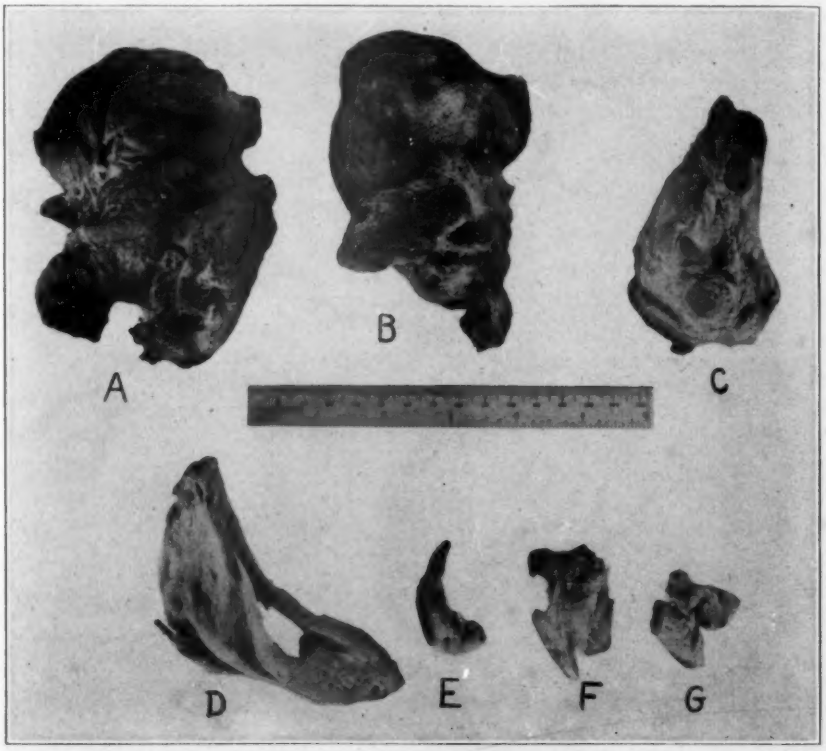

Fig. 1.—*A*, parosteal bone from left innominate bone denuded of fibrous capsule, weight, 450 gm., measurements, 15 by 10 by 10 cm.; *B*, parosteal bone from left femur denuded of fibrous capsule, weight, 290 gm., measurements, 12 by 9.5 by 7 cm.; *C*, parosteal bone from right thigh with fibrous capsule intact, weight, 100 gm., measurements, 8.5 by 5.5 by 4 cm.; *D*, parosteal bone from left thigh denuded of fibrous capsule, weight, 65 gm., measurements, 12 by 5 by 1.3 cm.; *E*, parosteal bone from left thigh denuded of fibrous capsule, weight, 5 gm., measurements, 4.5 by 2.5 by 1 cm.; *F*, parosteal bone from left thigh denuded of fibrous capsule, weight, 20 gm., measurements, 5 by 3.5 by 2.5 cm.; *G*, parosteal bone from left thigh denuded of fibrous capsule, weight, 10 gm., measurements, 3.5 by 2 by 1.5 cm.

7. Bard, L.: Manual d'anatomie, 1891, p. 317.

8. Graf, E.: Die konigliche Reserve Lazarethe zu Düsseldorf wahrend des Kriegen, Elberfeld, 1872, p. 64.

the rabbits bone formation in the center of the muscle. The results were inconstant.

4. The theory of subperiosteal dissemination of Berndt,[9] who holds with Macewen [10] that the periosteum is a limiting membrane and that when ruptured it allows the subperiosteal osteogenetic cells to proliferate and invade the musculature.

5. The hematogenous infectious myositis theory also advanced by Berndt [9] because in certain cases there is a slight rise in temperature, and the part becomes red and swollen, or else the bone formation may follow repeated abscesses.

6. The synovial theory of Ewald,[11] who considers the synovia as escaping into the soft parts, organizing and ossifying. He states that in the vast majority of cases bone formation in muscle occurs near joints.

7. The metaplastic theory of Orth,[12] who believes that intramuscular connective tissue by cell metaplasia is transformed into bone in the same manner in which the subperiosteal osteoblasts form bone. By tissue metaplasia he says that bone is formed directly from the connective tissue fibers.

8. The combined periosteal and metaplastic theory of Frangenheim [13] and Konig,[14] who assume that the intramuscular adherent bone is formed directly by the periosteum and by the metaplasia of the intramuscular connective tissue. Later on the continuity between the misplaced intramuscular bone and the true skeleton may be dissolved, leaving the parosteal bone free in the muscles.

9. Finally, Painter,[15] summing up all of the evidence at hand in support of the various theories advanced, comes to the conclusion that in the progressive, severe traumatic type and in myositis ossificans, resulting from slight but oft repeated irritations, the factor is a matter of diathesis or dyscrasia in varying degrees, which underlies them all. This is the only pathogenetic theory, he states, which will cover all cases. Marshall [16] comes to the same conclusion.[17]

---

9. Berndt, F.: Arch. f. klin. Chir. **65**:235, 1902.
10. Macewen, W.: The Growth of Bone, 1912, p. 33.
11. Ewald, P.: Zentralbl. f. Chir. **37**:771, 1911.
12. Orth, J.: Berl. klin. Wchnschr. **43**:430, 1906.
13. Frangenheim, P.: Arch. f. klin. Chir. **80**:445-450, 1905.
14. König, F.: Arch. f. klin. Chir. **80**:64-80, 1906.
15. Painter, C. F.: Boston M. & S. J. **185**:45 (July 14) 1921.
16. Marshall, H. W.: Boston M. & S. J. **184**:380 (April 14) 1921.
17. No attempt will be made in this paper to give a review of the literature or a critique of these various theories. A good summary of this subject will be found in the papers by Josephson, Cahier, Schulz, Jones and Morgan, Macewen, Painter and Fay (Surg., Gynec. & Obst. **19**:174-190, 1914), who first suggested the term "parosteal" for bone masses formed in muscle following trauma.

The clinical results following an injury that lead to intramuscular bone formation are usually swelling, induration due to hemorrhage and infiltration of muscles with blood, more or less complete loss of function and usually severe pain on pressure. According to Fay,[18] "Under treatment these symptoms grew less marked, but the functional does not keep pace with the objective improvement, and the doughy mass representing an extravasation of blood is found to be indurated sometimes as a whole, sometimes in scattered, circumscribed areas. The

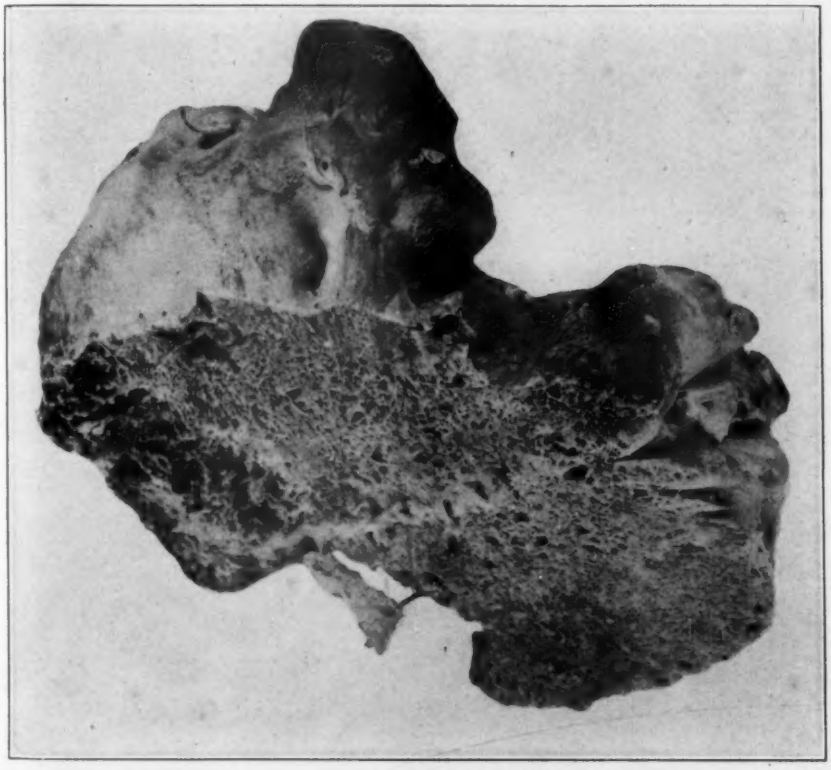

Fig. 2.—Parosteal bone of left innominate bone of fibrous capsule, weight, 450 gm., measurements, 15 by 10 by 10 cm. The surfaces produced by sawing have marrow spaces of various dimensions up to 1 cm. in diameter. The subcapsular caverns are well defined.

impairment of function continues to increase for some weeks, and the induration becomes more marked until it is of bony hardness." According to Machol,[19] these are the inevitable steps leading to ossification in uncomplicated reduced posterior dislocations of the elbow.

18. Fay, O. J., Footnote 17, p. 186.
19. Machol, A.: Beitr. z. klin. Chir. **56**:775, 1908.

REPORT OF CASES

History.—E. S., a negro teamster, aged 44, was admitted to the service of Dr. D. C. Strauss, at the Cook County Hospital, July 7, 1922, complaining of pain in the lower abdomen, scrotum, penis, hips and thighs, and inability to walk. He stated that, Sept. 8, 1921, while he was loading a wagon in a gravel pit, the bank caved in on him, crushing the pelvis and genitals. After the injury he was removed at once to a hospital, where he was bedridden for thirty-eight weeks. He was then taken home for three weeks. Since the accident he had lost 75 pounds and had been very weak.

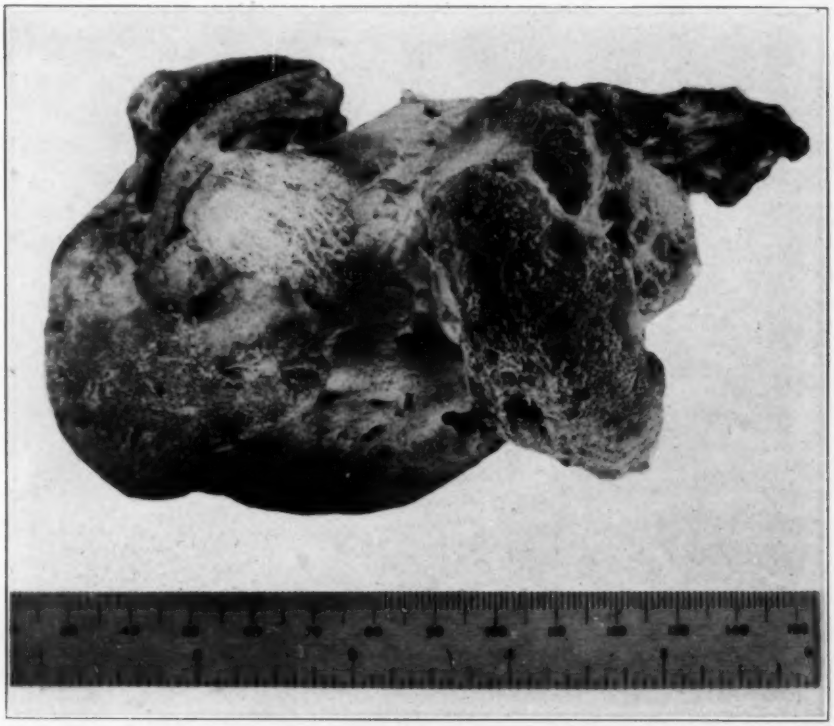

Fig. 3.—Parosteal bone from left femur denuded of fibrous capsule, weight, 290 gm., measurements, 12 by 9 by 5.7 cm. The dark arch cleft in the upper left corner is the area from which a segment was sawed out and sectioned for histologic examination. The compact bone is present in some places, on others the cancellous bone extends directly to the external surface. The porosity of this bone is clearly seen.

Physical Examination.—The patient was markedly emaciated, with a temperature of 98 F.; pulse, 102, and respirations, 18. The pain in the lower abdomen, penis, scrotum and thighs had been present constantly since the injury, Sept. 8, 1921, and was intensely aggravated when he moved in bed. There was a deformity of the left side of the pelvis, which had been present since the injury. The left iliac crest was rough, jagged and nodular but not tender. The upper and lateral part of the left thigh was swollen

Fig. 4.—Parosteal bone from right sartorius muscle with fibrous capsule up to 5 mm. thick, intact; weight, 100 gm., measurements, 8.5 by 5.5 by 4 cm.

Fig. 5.—Parosteal bone from left thigh denuded of fibrous capsule; weight, 65 gm., measurements, 12 by 5 by 1.3 cm.

and hard. Incontinence of urine and feces had existed from the time of injury. The penis and scrotum were swollen, tender and inflamed. There was marked atrophy of the muscles of the lower extremity. The left leg was completely paralyzed, the thigh was abducted, and the foot rotated outward. The knee jerk and Babinski sign were absent. The right leg could be flexed on the thigh, but the muscles were markedly atrophied. The knee jerk was present, but the Babinski reflex was absent. He died, Aug. 21, 1922.

Fig. 6.—Photomicrograph of proliferating cells connected with a small parosteal callus (Fig. 1 *E*), arranged along blood vessels and around scattered places of hemorrhage; × 30.

Necropsy Findings (Dr. E. R. LeCount).—Anatomic Diagnosis: "Parosteal bones of both femurs and left innominate bone, comminuted healed fractures of both femurs and left innominate bone; marked generalized anemia; marked emaciation; partly dehydrated body; anasarca; edema of brain and leptomeninges; suppurative and gangrenous balanitis; mucopurulent cystitis (urinary); ascending suppurative ureteropyelonephritis; decubitus ulcers of both buttocks and sacrum.

"The bony framework of the lower extremities is asymmetrical. The left leg is 89, and the right, 92 cm. long. The head of the left femur is displaced from the acetabulum; the thigh is abducted, and the left foot everted. The pelvis is tilted so that the left side is more caudad than the right. There is a bony hard mass of the medial and ventral surfaces of the left iliac bone, 13 cm. vertically by 6.5 from side to side. There are irregular bony masses of the front of the left thigh. Some are attached to the femur; others are free in the muscle. The entire group form a mass, 10 by 10 by 9 cm. In

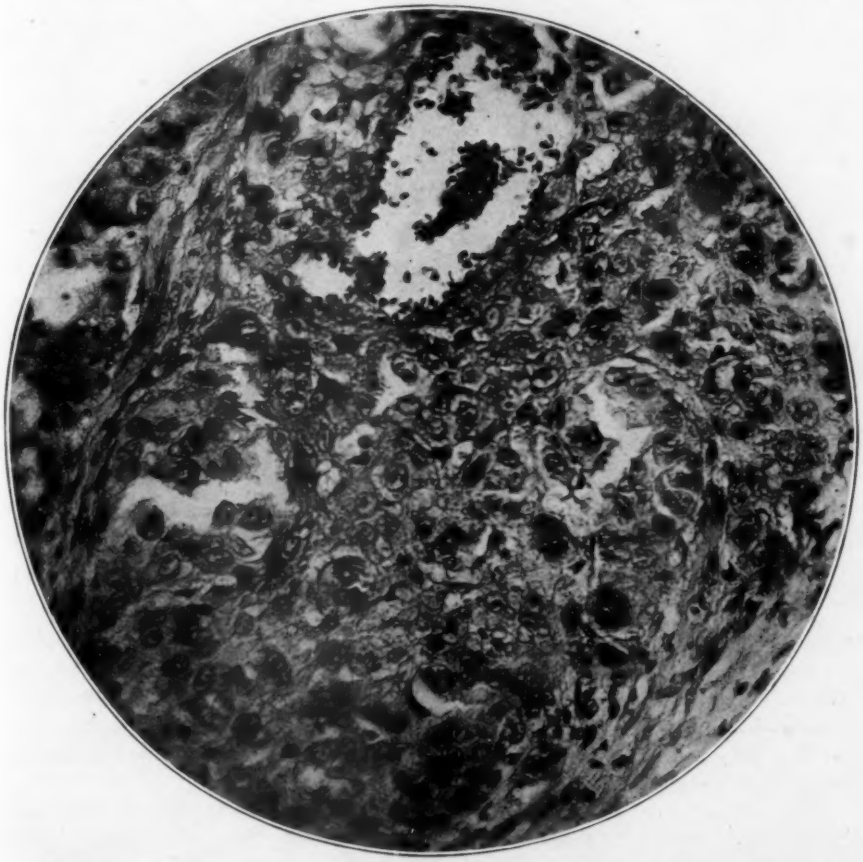

Fig. 7.—Photomicrograph of proliferating cells arranged along blood vessels; ×240.

the front of the right thigh, there is a similar mass, 5 by 5 by 4 cm., which is free in the sartorius muscle near the right anterior superior iliac spine. There is a callus of an old fracture of the upper third of the right femoral shaft, 8.5 cm. vertically by 2.5 wide and elevated 0.5 cm.

"On the left femur there are two masses, 28 cm. above the articular surface of the knee. One is 11.5 cm. vertically, 8.5 wide, and projects 6 cm. and is located ventromesially. The other is cephalad and is 15 cm. vertically, 2 cm.

wide and projects ventrally 5.5 cm. The bony mass of the left anterior superior iliac region has the following dimensions: 11 by 12 by 8 cm.

"On surfaces made by sawing across this mass it is seen to project internally from the left iliac fossa. The iliac bone is clearly demarcated. Both the tumor and ileum have a corresponding texture. On a surface of the larger tumor mass of the left femur made by sawing, two distinct parts are seen, one ventral, the other dorsal, and these are separated by a small amount of soft tissue into which the knife may be easily inserted. This tumor mass is like ordinary bone but appears to be a little more red. The head and neck of both the left and right femurs, respectively, are uninjured."

Gross Anatomic Examination: Six irregular masses of bone were taken from the left thigh and one irregular pyramidal mass from the right. The two largest ones (Fig. 1 *A* and *B;* Figs. 2 and 3) were attached to the greater trochanter of the left femur, and their projecting irregularly rounded surfaces were embedded in the gluteal muscles and fascia. The four smallest ones (Fig. 1 *D, E, F* and *G;* Figs. 4 and 5) were entirely embedded in the thigh muscles and had no osseous continuity with the skeleton. The largest parosteal

TABLE 1.—*Weights and Measurements of the Seven Pieces of Bone*

Figures	Thigh	Sept. 3 Weight Gm. Fresh	Oct. 16 Weight Gm. Dry	Dimensions, Cm.	Shape
1 and 8	Left	450	125	15 × 10 × 10	Irregularly quadrilateral
2 and 9	Left	290	75	12 × 9.5 × 7	Irregularly oval
3 and 10	Right	100	29	8.5 × 5.5 × 4	Irregularly pyramidal
4 and 11	Left	65	18	12 × 5 × 1.5	Irregularly arched
5	Left	5	1.0	4.5 × 2.5 × 1	Irregularly arched
6	Left	20	4	5 × 3.5 × 2.5	Irregularly quadrilateral
7	Left	10	2	3.5 × 2 × 1.5	Irregularly quadrilateral

bone (Figs. 1 *A* and 2) when stripped of muscle, fascia and fibrous capsule measured 15 by 10 by 10 cm. and weighed, Sept. 3, 1922, while still fresh, 450 gm., and when dried, Oct. 16, 1922, 125 gm. The smallest piece (Fig. 1 *E*) measured 4.5 by 2.5 by 1 cm. and weighed while still fresh 5 gm. and when dried, 1 gm., on the dates mentioned above. The data of weights and measurements of the seven pieces of bone are given in Table 1.

The internal arrangement of the cancellous trabeculae was clearly illustrated in surfaces produced by sawing (Fig. 2). The intertrabeculae spaces were from 0.25 to 10 mm. in diameter. The trabeculae measured grossly from 0.2 to 1 mm. in thickness, and, although irregularly arranged, there was a tendency for them to radiate from various centers and to intersect the external surfaces of the variously rounded trabecular eminences at right angles. There was a marked deficiency of cortical compact bone in some places; but in certain localities it was from 0.5 to 10 mm. thick. The unattached surfaces of the largest bony mass were conspicuously cavernous or spongiform (Fig. 2), and the finer meshwork pattern was visible where the compact bone was absent.

The smaller trabecular spaces on the surfaces produced by sawing, and the larger, cavernous, porous places on the free surfaces of the bony masses were filled with a doughy elastic brownish red vascular tissue which was easily

dissected out by gentle traction. In some of the largest caverns in the bone, there was a dark red friable mass resembling old coagulated blood.

Each mass of parosteal bone possessed a well defined connective tissue capsule with a maximal thickness of 8 mm. There was little difficulty in denuding the bone of this capsule. It was elevated with as much ease as the periosteum of diaphyseal bone. The intramuscular fibrous epimysium as well as the intramuscular perimysium was directly continuous with this fibrous capsule.

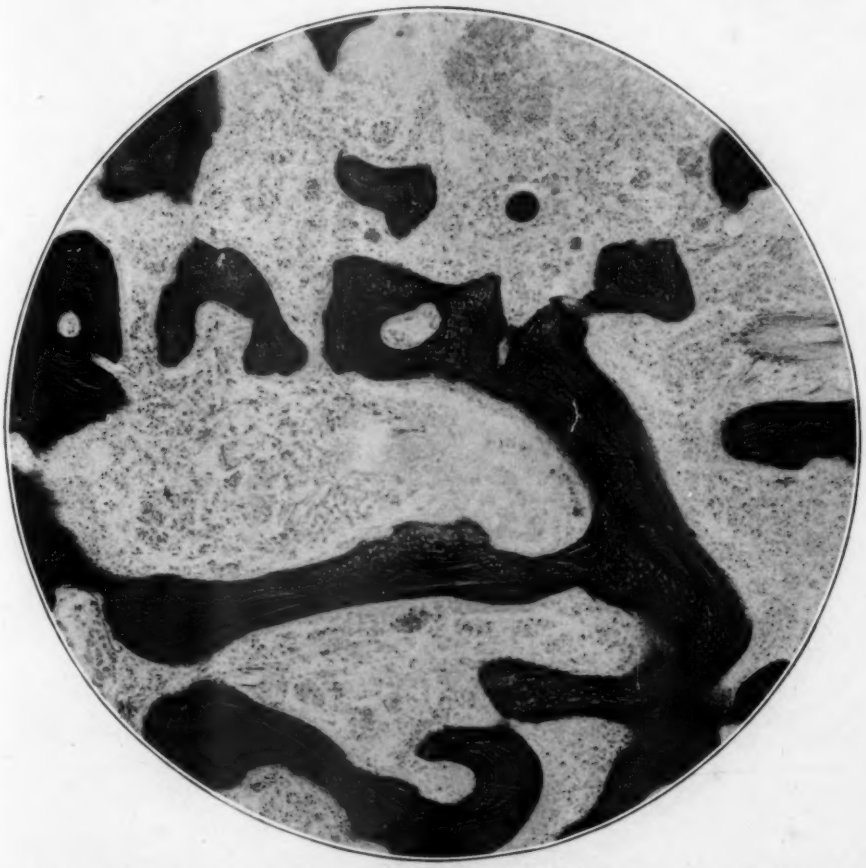

Fig. 8.—Photomicrograph of parosteal bony trabeculae with spindle and small round cells occupying the marrow spaces; × 30.

The smallest arch-shaped specimen (Fig 1 *E*) had a diagonal groove on its concave surface which contained a gelatinous, elastic, pale red tissue that measured 2 by 1.5 by 1 cm. and extended into the intermuscular fibrous tissue. This was dissected out, fixed in Zenker's fluid, embedded in paraffin, sectioned and stained with hematoxylin and eosin for microscopic examination. From this specimen (Fig. 1 *E*) there projected a bony mass, 3 cm. long, 2 wide, 0.5 thick, which was fixed in Zenker's fluid, decalcified, embedded in celloidin and stained with hematoxylin and eosin.

Histologic Examination.—Sections taken from the pale red gelatinous mass which was in the groove of the arch-shaped parosteal bone (Fig. 1 *E*) and extended into the intermuscular connective tissue were composed chiefly of small round cells with large nuclei. These nuclei contained an abundance of chromatin and in most cases nearly filled the cell (Fig. 7). Some of the cells appeared to be arranged in rows along the course of blood vessels, whereas others formed definite islands. The amount of interstitial tissue was variable. In some localities the cells were closely packed together, while in

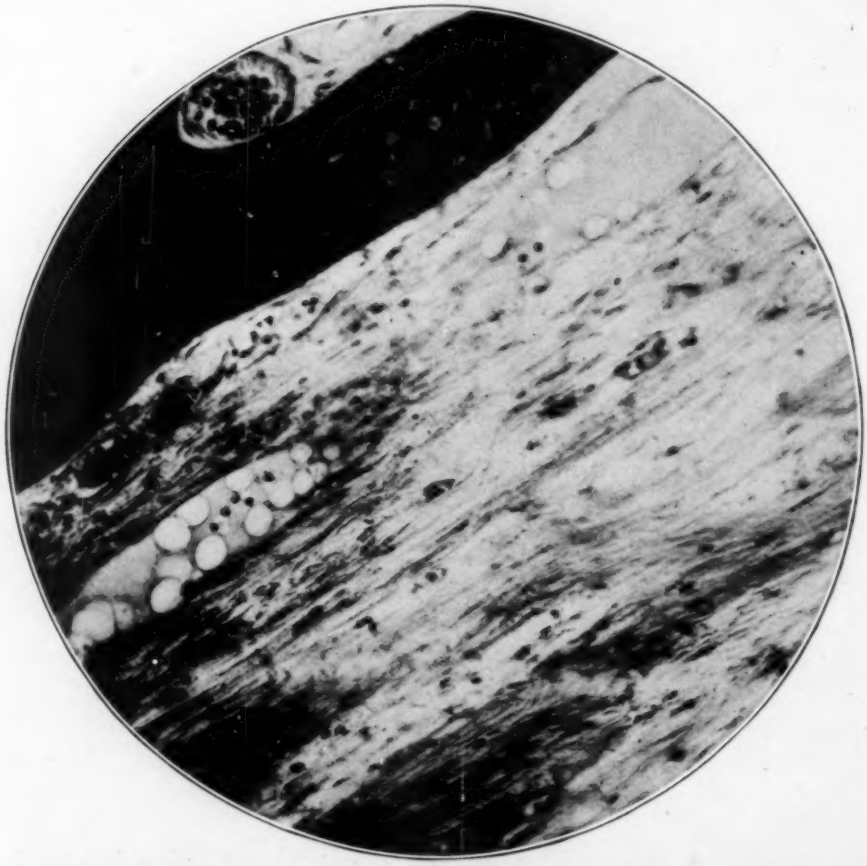

Fig. 9.—Photomicrograph of parosteal bony trabeculae with elongated spindle cells and fat occupying a large marrow space; × 100.

others they were widely separated by an abundance of reticulum. In all of the sections, trabeculae of connective tissue were seen extending into the proliferating mass from a thick capsule. Some of these trabeculae flared out into finer fibrils which coursed between the cells. Certain parts of the sections were more vascular than others, and the blood vessels were like thin walled sinusoids filled with red blood corpuscles. In all of the sections a hemorrhagic area, 1 mm. in diameter, was seen around the periphery, in which there was brownish red pigment. There was evidence of scattered areas of hemorrhage in all of the sections of the brownish red pigment. (Fig. 6).

The intermuscular connective tissue, as well as a fragment of muscle, was invaded by the proliferating round cells. The walls of some of the larger and smaller blood vessels were also infiltrated with these cells. The lumen of many of the smaller blood vessels was filled with blood and many round cells, some of which were polymorphonuclear leukocytes.

Segments of the parosteal bone were decalcified, sectioned and stained with hematoxylin and eosin. Sections from a number of places were studied. One place in particular appears as a gap in Figure 3, and in a general way they all correspond to the following description. In some places there was more bone than in others. There was slight evidence of cartilage in the center of certain bony trabeculae. The bony trabeculae were thicker close to encapsulating fibrous tissue. The trabeculae of bone varied in width up to 1 mm. In the center of certain larger trabeculae there were larger lacunae with blue capsules around which the bone had grown. These were best seen in the narrowest and smallest trabeculae. They were not present in the thickest trabeculae. There was no evidence of inflammatory changes. Certain marrow spaces contained spindle shaped cells and loosely aggregated collections of round cells (Fig. 8).

Some marrow spaces were large and possessed considerable fat (Fig. 9) and sinusoidal-like blood spaces. In other spaces there were densely packed round cells. Sections from the largest masses of parosteal bone contained unusually large marrow cavities with many large round spaces up to 0.15 mm. in diameter where fat formerly was present.

Sections of the projecting bony mass continuous with the smaller arch-shaped specimen (Fig. 1 E), which also contained a gelatinous elastic pale red tissue in a groove on its concave surface, had compact and cancellous bone. A great portion of the bone marrow had been replaced by tissue resembling the gelatinous pale red tissue mentioned above. In some places there was a small portion of fatty tissue, but connective tissue stroma was invaded here also by small round cells.

CONGENITAL CYSTIC DILATATION OF THE COMMON BILE DUCT

REPORT OF A CASE, WITH CURE

GOLDER LEWIS McWHORTER, M.D., PH.D.

CHICAGO

The case here reported illustrates an unusual condition of intermittent obstruction with cystic dilatation of the common bile duct. Because of one proved congenital case and the fact that the onset occurs frequently in childhood, this condition is classified as congenital.

Failure, in the past, to recognize this type of obstruction and to provide internal drainage has resulted in an operative mortality of 71 per cent. All cases in which operation was not performed have resulted in death.

REPORT OF CASE

History.—Mrs. S., aged 49 years and 10 months, who entered the Presbyterian Hospital, Nov. 16, 1922, complained chiefly of recurrent pain in the right upper quadrant with severe exacerbations and colic, associated with nausea and vomiting; jaundice with the severe attacks of pain, and inability to eat more than a scanty diet, because of the resultant pain.

The patient was born in Holland. According to her mother, from the age of 6 months she had had attacks of distress in the abdomen with difficulty in eating. She suffered from jaundice, which at these times, was more marked and which did not clear up until she was 7 years old. During the attacks, she would lie doubled up with her face down. She was a thin and delicate child and was never able to run about and play. Most of the time, she did not attend school, since it was difficult for her to sit down for any length of time because this brought on the attacks of pain.

During the second period, from the age of 7 years until her first pregnancy, at the age of 19, there was less distress, and the attacks of pain were less severe than they had been before or since. However, she was never able to eat large meals, and could eat only a limited number of things. There was jaundice with these attacks but it did not persist and was not so severe during this period.

The third period covered her child-bearing. During each pregnancy, the attacks became much more severe about the fourth month, but were not more frequent. The pains were much worse after the seventh child.

The fourth period covered the last year. Her menses became irregular four years previously and one year previously ceased. The patient dated the onset of greater distress from this cessation. The pains had become worse and the severe disabling attacks were more frequent, coming about every three or four weeks.

The pain started in the epigastrium, extending to the region of the right upper quadrant, and radiating to the back and the lower angle of the right scapula. The pain sometimes grew more severe until the patient vomited. During the severe pains, she felt cold and sometimes had chills which were followed by a sensation of heat, and then by perspiration. As far as she knew, she had had no fever, and the feverish feeling passed away with the pain.

The attacks usually occurred after eating, but they also came on when she was at work, even when there was no food in the stomach. They usually began after meals when she started to do her housework. She might vomit bile or, if the pain came on soon after eating, she might vomit food. The attacks never began at night. They usually developed about 10 or 11 a. m. and would gradually get worse until about 3 or 4 p. m., when they were usually the most severe. The patient sometimes obtained relief if she immediately drank hot water. At times, the hot water bag gave relief. In the severe attacks, the pain grew worse about 3 or 4 p. m., and she would have to double up on the floor and remain there until about 7 or 8 o'clock. The severe pain would then gradually subside; but for the last fifteen or sixteen years, she had a hypodermic when they persisted. She had taken these injections three or four times a year for the last sixteen years, but much more frequently during the last year.

The stomach and the whole upper part of the abdomen felt full and tender during an attack, and she could not eat anything; but she had never noticed any mass. She was constipated after the attacks, and there was usually a clay color to the stools during the severe attacks. Jaundice usually occurred, and there was a marked yellow color to the skin, which lasted for two or three days and was accompanied by a marked itching over her body. She would have a headache, feel miserable and have a feeling of soreness in the upper part of the abdomen. This soreness would disappear gradually, in two or three days.

During the last attack, a week previously, all of the severe symptoms were present. The patient, who was doubled up on the floor, was apparently suffering more severe pain than is present in the ordinary case of gallstone colic. There was slight but definite jaundice for three or four days after the attack.

Ordinarily, the bowels moved once a day, without cathartics. The appetite was rather poor, and the patient was afraid to eat ordinary food. Many times she would go to the table and fearing that she would suffer distress would, instead of eating the food prepared, drink a cup of tea and eat a piece of bread. Her ordinary meals were: breakfast: bread or toast, tea or milk and a cereal; lunch: bread, tea or milk and perhaps a pudding; supper: a hot pudding, bread and butter and tea or milk.

Since childhood she had been able to eat very little, and anything unusual would bring on attacks of pain. While the severe attacks came on at intervals of from a week to one or two months, she was never free from some distress after eating a meal of any sort. A large meal or the eating of certain things made the pain worse until perhaps she would develop a severe attack, which would not be relieved by drinking hot water, by the use of a hot water bag or by vomiting.

The following foods were not eaten because they caused pain: potatoes in any form, meat, eggs, cabbage, radishes, beans, practically all vegetables, coffee, apple pie, apples, all seeded things and cheese.

Foods that did not seem to bring on the pain if eaten in small amounts were: carrots, spinach, oranges, almost all sour things, such as pickles and sauces, prunes, cereals of all kinds, milk, tea, rice, tapioca and butter. She was always afraid to eat sweet things, but she thought that they did not bring on the attacks.

There had been no other illness. She did not have the infectious diseases that the other children in the family had.

The menses began at the age of 12 years, were regular, every twenty-eight days, and attended by a good deal of pain. When the attacks occurred at this time, the jaundice and the upper abdominal pains were usually worse. The patient married at the age of 19 years, and had nine children. The oldest was 30 years old; the youngest, 11. The children were all well. There had been one miscarriage between the last two children, at three months. The menopause began four years previously. The periods were irregular until one year before, when they ceased.

The patient's mother died at the age of 65, from a paralytic stroke. Her father died at the age of 75 from pneumonia, the past year. She had three brothers and four sisters, all well.

An operation had been performed fourteen years before, because of the severe attacks, which she continued to have. At the operation, the gallbladder was drained. The patient's husband stated that no stones were seen. The appendix was not removed. The operation was performed when the eighth child was about 2 years old. Just before leaving the hospital, when the drainage had practically stopped, the patient had one of her typical attacks of pain. Following this, the attacks occurred as before.

Physical Examination.—The patient was a small and slight woman, apparently about 50 years old, not acutely ill. The present weight, 95 pounds (43.2 kg.) was about her average weight.

The skin was bronzed or copper colored. There were several large areas of dark brown pigmentation on the body, and the forearms were quite covered with brownish pigmented areas and spots. There was definite yellowing of the conjunctiva for three or four days after the last attack, with a deeper yellowish tinge over the whole body.

Examination of the head and chest was negative. Examination of the heart revealed an occasional extrasystole.

There was a short scar about 2 inches (5 cm.) long over the region of the gallbladder, which was dimpled over the upper part. The abdominal wall was generally relaxed and redundant below, but it was rather rigid over the right upper quadrant, and it was difficult to palpate the region deeply. The liver and spleen were not palpably enlarged. There was a vague palpable mass in the right upper quadrant, which was thought to be the right kidney. The muscle rigidity and tenderness prevented outlining any definite mass or tumor.

The extremities were negative except for pigmentation. The reflexes were normal.

Laboratory Findings.—The urine was negative except for the presence of bile after the acute attack. The blood pressure was 132 systolic, 60 diastolic during the attack. One week later, it was 178 systolic, 110 diastolic. The pulse was 72. There was no fever at any time during observation or during the last attack.

An Ewald test meal was withdrawn at forty minutes, and 60 c.c. was obtained, one-half solid and finely divided. The total acid was 75; free acid, 55; combined acids, 20.

A motor meal was aspirated after seven hours, 30 c.c., grayish green, with possibly a small amount of finely divided food substance. The total acid was 32; free acid, 25; combined acids, 7. No bacteria were seen. The blood test was negative.

Roentgenograms of the urinary tract and the gallbladder region were reported by Dr. Rose. On the right side, at the level of the first lumbar region, was an irregular dense shadow, the chief portion of which extended about 1.5 cm. in

each direction. From the lower border, extending toward the spine, was a string of tiny dense areas of calcification. The possibility of calcification in the pancreas was suggested.

A diagnosis of obstruction of the common bile duct probably due to stones was made.

Operation (Nov. 7, 1922).—The abdomen was opened mediad to the old scar, and many adhesions were found around this region. When they were freed from the peritoneum, a sac containing bile was opened, which was thought to be a rather small elongated gallbladder. This led to the dilated cystic duct and a large dilated common duct. The cystic duct was incised and about a pint of clear bile poured out. The incision was extended into the common duct, which was now seen to be cystic and spherical below. All attempts to find an opening from within leading into the duodenum failed, and the sac was then dissected from behind the duodenum, to which it was adherent. During this dissection, a short stump about 1 cm. long was broken away from the sac wall. It extended out from the posterior wall of the duodenum and was not surrounded by pancreatic tissue. I made a brief attempt to probe this cordlike structure, thinking it might be the terminal duct; but I did not find the lumen. The sac was freed up to the liver (Fig. 1) and both it and the gastrohepatic omentum were explored carefully for a duct leading into the duodenum. There were a few black, bird-shot sized stones in the sac. On exploring above, my finger easily passed into dilated branches of the hepatic duct, which were partly filled with these small stones. A large number of these were removed with a scoop. The liver appeared normal in size, but it was dark, quite friable and bled more freely than normal. Since the opening into the duodenum from the cystic choledochus had been incompletely draining bile and was now apparently torn away, an anastomosis was necessary to the duodenum. The pancreas was entirely to the left of the duodenum, and there were several large calcareous masses palpable in its head, which was firm and seemed rather sclerotic, but was without evidence of inflammation.

The duodenum was mobilized, and the posterior side of the hepatic duct was sutured to the side of the duodenum about 4 inches (10 cm.) from the pylorus. The sac and the gallbladder, which had been used for traction, were now cut away. An opening was made in the duodenum about 2 cm. long, and the anastomosis completed with two rows of plain catgut sutures. Two sutures fixed the duodenum to the round ligament of the liver in order to relieve the tension on the suture lines. Two small cigaret drains were put in near the anastomosis.

Pathologic Examination.—The specimen was quite shriveled owing to the action of the fixing solution. The sac was globular at the duodenal end and narrowed above to the dilated hepaticus.

The sac measured 10 cm. from the upper cut end to the lower globular duodenal end. Its width was 6 cm. The upper end, where it joined the hepatic duct, measured almost 2 cm. in diameter. The gallbladder was also shrunken, but the wall was thickened. It measured 4 by 2 cm. The stones were black, rather soft and slightly irregular but shotlike. There was about one-half ounce of them. They gave a positive reaction to tests for cholesterin and bile pigments.

There was an opening at the fundus of the gallbladder where it was freed from the old scar. The neck of the gallbladder had a very thick spincter-like muscle (Fig. 1 *A*). The upper part of the cystic duct was not dilated, but the lower portion was widely dilated. The inside of the sac was fairly smooth except for some rather superficial trabeculations. There were two

small pinhead sized openings in the spherical duodenal end of the cyst. One of these presumably was at the junction of the terminal extraduodenal bile duct and the sac, but there was no change in the sac around the opening. The other opening may have been traumatic, or it may have been a saccule filled with a pinhead sized mass of soft soaplike material which was exposed at one point while the sac was being dissected.

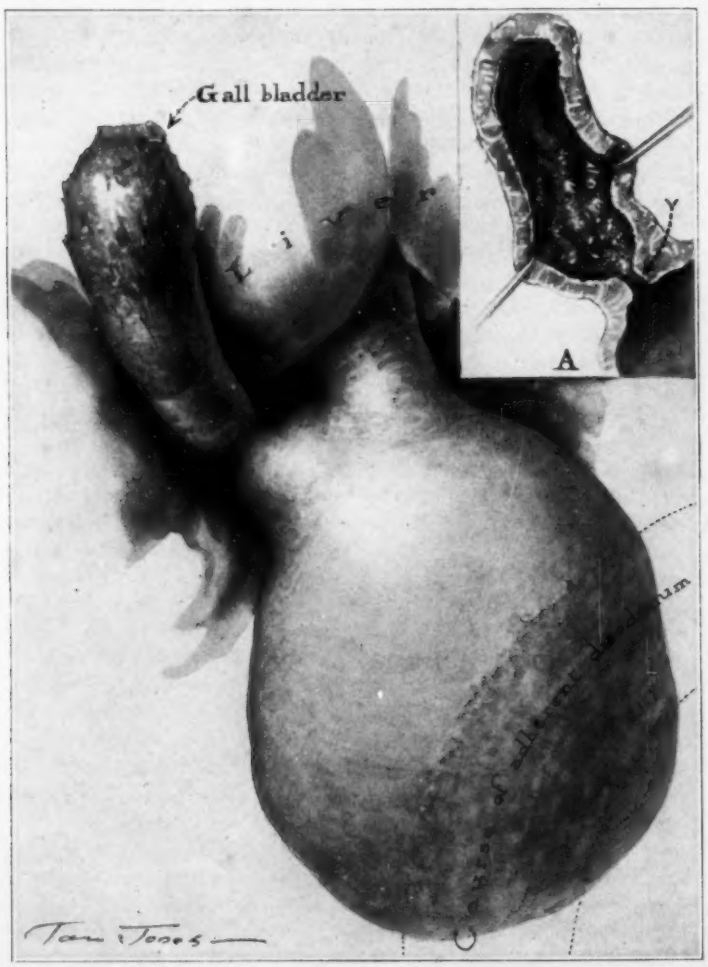

Fig. 1.—The cyst extends down from the dilated hepatic duct to behind the duodenum. A short narrow friable duct attached to the duodenum was torn away from the cyst wall, and its location is not shown. The arrow indicates old adhesions about the gallbladder. The cystic duct is widely dilated below. *A*, a markedly hypertrophied sphincter muscle at the neck of the gallbladder.

Microscopic Examination.—The cyst wall which varied somewhat in thickness, was composed of fibrous connective tissue. There was an inner dense layer of fibrous tissue composing about one half the wall. There was a middle layer

of more loosely arranged fibers, forming about one fourth the wall and an outer layer of connective tissue which was rather vascular (Fig. 2). There was an absence of mucosa, of epithelium and of muscle fibers. In the sections stained by differentiated tissue stains, there was an absence of yellow elastic tissue except around the blood vessels. In only one section, near the middle of the cyst wall, were seen the cross sections of three or four tubules, lined with low cuboidal epithelium. They were surrounded by some circularly arranged fibrous tissue.

A fragment of liver attached to the gallbladder appeared to be congested. There were many round and polymorphonuclear cells. The strands of liver

Fig. 2.—A section of the cyst wall. There are dense layers of fibrous connective tissue on the inside and more loosely arranged layers externally. There is complete absence of an epithelial layer.

cells were swollen and the lobular character was almost lost. Many of the liver cells stained poorly, and there appeared to be a good deal of blood throughout the tissue. There was apparently no increase of connective tissue.

The gallbladder wall was thickened, owing to hypertrophy of the muscle layer and some connective tissue thickening. The epithelium was high columnar, but there were areas where it was absent. There was some round-cell infiltration and a few polymorphonuclears in the submucosa.

Postoperative Course.—Convalescence was uninterrupted except for a temporary duodenal fistula which began on the twelfth day with a discharge of

chyme. The skin was never excoriated by the discharge, and the patient continued to gain in strength. This discharge lessened after a few days, and stopped in about two weeks. Following the operation, the patient was able to eat any kind of food for the first time in her life, she said, without distress or pain.

Roentgenograms were taken twenty-five days after operation. Barium sulphate given by mouth was seen passing readily into the duodenum and the cap appeared to be of good size. Just below this, the barium extended upward in a peculiar branching shadow, apparently in the hepatic bile ducts.

A second film showed that the ramifications extended a little farther outward toward the right. A catheter could be inserted into the external sinus about 2 inches (5 cm.) and extended beyond the duodenal cap. A film taken five hours after the first examination revealed only traces of barium sulphate in the region described before. Most of the barium was seen in the ascending and first part of the transverse colon. The appendix was filled with barium.

A film taken eight hours later showed a spider-leg type of filling of the smaller ducts of the liver still present.

A film taken twenty-four hours later revealed only traces still present in the liver region.

Roentgenograms taken one year later showed a similar filling of the bile ducts with barium sulphate.

On examination, October 25, 1923, one year later, the patient was still perfectly well and was doing all of her housework. She was able to eat everything. She had had no pain and had gained 20 pounds (9 kg.) since the operation. The pulse was 72; blood pressure, systolic 170, diastolic 85. The abdomen was negative to palpation.

THE LITERATURE

The following study of the reported cases of this condition includes practically all cases accepted by any previous writers. I have read all the original articles with the exception of Smit's,[1] which was not available. When there was a definite pathologic condition explaining any obstruction, such as congenital atresia, pancreatitis, stone or inflammatory stricture, the case was not included.[2] There seemed

1. Smit: Et tilfaelde af idiopatisk choledochuscyste, Med. Rev., Haarlem **32**:285, 1915; quoted by Waller.

2. Barloch: Deutsch. med. Wchnschr. **31,** 1876. Bazy, P.: Choledochoduodenostomie pour obliteration de la portion terminale due choledoque, Bull. Acad. de med. **75**:137, 1916. Eve: Large Cyst of the Common Bile Duct, Brit. M. J. **1**:802 (April 7) 1906. Exner: Wien. klin. Wchnschr. **25**:469, 1912. Fowler, R. S.: Choledochus Cyst, Ann. Surg. **64**:546, 1916. Frerichs: Diseases of the Liver, London, New Sydenham Society **2**:469, **1861**. Kehr, H.: Chirurgie der Gallenwege, Neue Deutsch. Chir. **8,** 1913. Legg, J. W.: Congenital Deficiency of the Common Bile Ducts Ending in a Blind Sac; Cirrhosis of Liver, Tr. Path. Soc., London **178,** 1876. McConnell, G.: Cystic Dilatation of Biliary Ducts, Proc. Path. Soc., Philadelphia **16**:12, 1914. Mayo-Robson: Diseases of the Gallbladder and Bile Ducts, Ed. 3, 1904. Milner, S. W.: Brit. M. J. **1**:1235 (May 22) 1909. Oxley, M. G. B.: Congenital Atresia of the Duodenal Opening

(Footnote 2 continued on next page)

insufficient evidence for including several of the cases in this paper; such as, Arnison's,[3] with practically no data, and Lavenson's,[4] the only one in which complete obliteration of the terminal duct was found; but these have been accepted by recent writers, and I have therefore included them. I believe that Sternberg's [5] necropsy report must be on the case reported by Bakes [5] in which operation was performed, and it is so considered in this study, although Waller [6] reports them as separate cases.

Etiology.—The etiology may be a specific one or must consist of numerous predisposing factors any one of which may lead to the cystic dilatation of the common bile duct. There is the possibility of either a congenital or an acquired dilatation. The majority of authors believe in some congenital anomaly.

Heiliger's [7] case proves that congenital dilatation of the choledochus does occur. He believes it is primary in the wall of the choledochus, and suggests that either the wall is redundant or abnormally weak, although the distal end was narrowed. Dreesmann [8] believes in a congenital weakness of the wall with subsequent dilatation.

---

of the Common Bile Duct in an Infant, Producing a Large Abdominal Tumor, Lancet **2**:988 (Dec. 8) 1883. Outerbridge, G. W.: Proc. Path. Soc., Philadelphia **14**:174, 1912. Raynaud and Sabourin: Note sur un cas d'énorme dilatation des voies biliaires; avec periangiocholite chronique et hypertrophie des glandes pericanaliculaires, Arch. phys. norm. et pathol. **16**:36, 1879. Reynier: Valeur diagnostique de l'état de la vesicule biliare dans les obliterations du canal choledoque, Bull. et mém. Soc. de chir. de Paris **18**:803, 1892. Sumpter, W. D.: Dilatation of the Common Bile Duct, South. Pract., Nashville **39**:169, 1917. Terrier: De la choledochostomie, Rev. chir., February, 1893, p. 81. Todd: Dublin Hosp. Rep. **1**:328, 1817; quoted by Legg: Brit. M. J. **1**:607, 1874. Wilkes and Moxon: Cited by Eve and Lavenson: Lectures on Pathological Anatomy, Ed. 3, p. 485, 1883.

3. Arnison: Cited by Mayo-Robson: Diseases of the Gall-Bladder and Bile Ducts, Ed. 3, 1904, p. 200,

4. Lavenson: Cyst of the Common Bile Duct, Am. J. M. Sc. **137**:563, 1909.

5. Sternberg: Diskussion zur typischen Erweiterung des Choledochus, Wien. klin. Wchnschr. **46**:1616, 1911. Blakes, J.: Kolossal dilatierter ductus choledochus, Idiopath. Retentionscyste. K. K. Gesellschaft der Arzte in Wien, Wien. klin. Wchnschr. **20**:298 (March) 1907; Choledochus retentionscyste, Compt.-rend. deux. Cong. Soc. internat. de chir. Bruxelles **1**:122, 1908; Discussion zur Choledochuscyste, 38 Deutsch. Chir. Kong., Verhandl. **1**:172, 1909.

6. Waller, Erik: Ett fall a operad idiopatisk choledochyscysta, Hygiea **79**:513 (June 16) 1917; Ann. Surg. **66**:446 (Oct.) 1917.

7. Heiliger, J.: Ueber die congenitale cystenartige Erweiterung des Ductus choledochus, Inaug. Dissert. Giessen, 1910.

8. Dreesmann: Angeborene Choledochuserweiterung, Deutsch. med. Wchnschr. **37**:1518, 1906; Beitrag zur Kenntnis der kongenitalen Anomalien der Gallenwege, Deutsch. Ztschr. f. Chir. **92**:400, 1908.

Lavenson, Ebner,[9] Dreesmann, Weiss [10] and Goldammer [11] assume a primary weakness of the wall. Ebner and Lavenson specify a weakness of the muscular tissue.

Lavenson thinks that the delicate walls of the bile ducts in the young are less able to withstand the pressure of the bile secretion than are these walls in adult life. But there must be additional reasons, he states, since cystic dilatation of the choledochus is not found in congenital obliteration of the bile ducts in which obstruction is in the lower end of the duct.

Kolb [12] believes that there may be a spindle-shaped dilatation dating from fetal life, as in cases of certain animals in which no gallbladder is present.

There may be a congenital narrowing of the duodenal part of the choledochus, as believed by Heid,[13] Seeliger [14] and Edgeworth.[15] Lavenson thinks the narrowing may result from inflammation, but other factors may be present causing obstruction. Others believe that the cause may be an abnormal course of the lower part of the choledochus (Cases 5, 11, 18, 42, 23, 46, 12, Table 1).

Konitzky [16] found an abnormal course, but thought a catarrh of the duodenum possibly produced an incomplete obstruction at the outlet of the choledochus.

Wettwer [17] believed the cause was due to the passing of the choledochus through the duodenal wall from below up instead of above down. Rostowzew [18] believed it was due to the choledochus passing through the duodenum from right to left instead of from left to right.

---

9. Ebner: Idiopathische Choledochuscyste und Purpura haemorrhagica fulminans, Beitr. z. klin. Chir. **64**:473, 1909; Ueber Choledochuscysten (Demonstration), Verhandl. d. deutsch. Gesellsch. f. Chir., 38 Chir. Kong. **1**:170, 1909.

10. Weiss, S.: Ein seltener Fall von cystischer Erweiterung des Ductus choledochus, Berl. klin. Wchnschr. **46**:1843 (Oct. 11) 1909.

11. Goldammer: Beiträge zur Chirurgie der Gallenwege, Beitr. z. klin. Chir. **55**:214, 1907.

12. Kolb, O.: Ein Fall von hochgradiger kystenartiger Erweiterung des Ductus hepaticus und des Ductus choledochus, Inaug. Dissert, München, 1906.

13. Heid, L.: Ein Fall von hochgradiger cystenartiger Erweiterung des Ductus choledochus, Inaug. Dissert. Giessen, 1893.

14. Seeliger, S.: Beitrag zur Kenntnis der echten Choledochuscysten, Beitr. z. klin. Chir. **99**:158, 1916.

15. Edgeworth, F. H.: Case of Dilatation of the Common Bile Duct Simulating Distention of the Gall-Bladder, Lancet **1**:1180, 1895.

16. Konitzky, G.: Ein Fall von hochgradiger cystischer Erweiterung des Ductus choledochus, Inaug. Dissert. Marburg, 1888.

17. Wettwer, E.: Ein Fall von congenitaler Choledochuscyste, Inaug. Dissert. Göttingen, 1907.

18. Rostowzew, M. J.: Ein Fall von hochgradiger cystischer Erweiterung des Ductus choledochus, Deutsch. med. Wchnschr. **28**:739 (Oct. 9) 1902.

Lavenson believed the angular insertion was the result and not the cause of the dilatation. In his case, there was obliteration of the choledochus; but in other cases in which the lumen was patent, he thinks that cholangitis or some temporary obstruction was primary and dilatation was secondary.

Abnormal or diminished anlage formation of the choledochus, with a diverticulum and cyst formation of the extraduodenal part was also considered as the cause (Cases 33, 36, 39).

Seyffert [19] believes that the passage of gallstones was a factor in his case.

Budde [20] believes that the cyst was the result of primary diverticula from pancreatic anlage, and similar to traction diverticula. He believes that the histologic findings of fibro-adenomatous structures in the wall of the terminal part of the choledochus supported this theory.

There are many theories having congenital malformation as a basis, upon which various factors are secondary.

Several assume as secondary factors mucosal swelling or duodenal catarrh, producing dilatation of an anomalous duct (Cases 15, 24, 12, 17, 46). Repeated attacks increase the dilatation. Edgeworth believed that a congenital stenosis of the choledochus favored attacks of catarrh with increasing obstruction.

Ebner and Rostowzew believed that secondary factors may be narrowing of the outlet not only by swelling of the mucosa but also by a reflex spasm of the sphincter of Oddi. Others mentioned as secondary factors the formation of a valvelike closure and kinking or an abnormal course of the lower part of the choledochus (Cases 2, 12, 22, 5, 21, 33, 23, 34, 39, 46). Incomplete or complete valve formation was present in several others (Cases 18, 45, 26, 15, 10, 6).

Fenger [21] states that the bending of the choledochus may be caused either by elongation of the ducts or by traction from adhesions. He believes that the obstruction in these cases is at first incomplete and that the intermittent attacks may result in either dilatation or hypertrophy of the ducts above. The bending, he thinks, is most likely to take place at the beginning of the duodenal portion of the common duct because there is a sudden change in the diameter at this point. He states that Virchow first drew attention to bending of the bile ducts with retention.

Goldammer thought that compression at the outlet of the common duct might be due to pregnancy, with stretching out of a weak wall,

---

19. Seyffert, R.: Cyste des Ductus choledochus, operativ behandelt, Inaug. Dissert. Greifswald, 1888.

20. Budde, Max: Ueber die Pathogenese und das Krankheitsbild der cystischen Gallengangserweiterung. Sogenannte idiopathische Choledochuscyste, Deutsch. Ztschr. f. Chir. **157**:364, 1920.

21. Fenger: Tr. Am. Surg. Ass'n **14**:699, 1896.

and to diverticulum formation. The fall in abdominal pressure following delivery, I believe, might cause an acute kinking with obstruction of the choledochus. In two other cases, the onset of symptoms developed during or immediately after a pregnancy (Cases 6, 43).

Roberts [22] stated that excess of the choledochus sac, with weakness and possibly a stenosis of the lower part, is probably the original anomaly. This predisposes to a kink, which produces the obstruction. However, he adds, the kink alone might produce the dilatation, aided by a catarrh or spastic sphincter of Oddi.

Pathology.—On opening the abdomen, one usually sees a large cystic tumor. However, frequent adhesions and the location behind the flexure of the colon and the duodenum prevent easy recognition of the condition.

The size of the cyst has varied from that of a man's fist to that of a full-term fetus. The contents have usually been clear bile, but in a few cases there was a purulent bile-colored fluid present. Russell [23] found white bile present.

Concretions: These were present in the dilated bile ducts in a few cases, including the one reported herewith. Dreesmann found two small fragments of stones. Goldammer found two somewhat larger than pinhead sized stones. Wagner [24] reported a few of the finest crumbling particles of sediment in the sac. Roberts found the dilated bile ducts to contain some masses of greenish black inspissated material, among which were a few little calculi of the same color and about the size of a pinhead.

Russell examined several black cinder-like masses from the white bile, and found that they consisted of crystals of bilirubin.

Arnolds [25] found the wall of the cyst partly encrusted with a sediment. In the case of Budde, there were several large depressions in the wall of the cyst whose bases were encrusted with sediment of bile pigment. There were encrustations on the wall in the case of Konitzky. Ebner reports that there were encrustations of the very finest concretions on the wall of the gallbladder in his case.

The cyst: The cystic dilatation was usually spherical, but it was sometimes pear-shaped, tapering above. The lower rounded part of the

22. Roberts, E. D.: Un cas de dilatation Kystique du canal choledoque, Thése, Lausanne, 1914.

23. Russell, R. N.: Case of Cystic Dilatation of the Common Bile Duct in a Child, Ann. Surg. **26**:692, 1897.

24. Wagner, A.: Beitrag zur Chirurgie der Gallenwege, Deutsch. Ztschr. f. Chir. **145**:15, 1918.

25. Arnolds: Mannskopfgrosse Retentionscyste des Choledochus, Deutsch. med. Wchnschr. **32**:1804 (Nov.) 1906.

cyst usually extended below the narrow terminal duct leading into the duodenum, which favors a valve compressive action on distention of the sac. The lower part of the sac extended nearly always to the right and posteriorly to the descending portion of the duodenum, so that the outlet lay on the medial side. Lavenson says that the lack of tension to the right of the duodenum permits dilatation of the bile duct more easily in this direction, with a resulting angulation of the outlet. In a few cases, the outlet into the duodenum was on the right side and the cyst seemed to have extended more to the left and posteriorly to the descending duodenum (Cases 10, 2, 47, 34).

The cystic dilatation involves the middle and upper part of the choledochus. In some cases, the hepatic duct was involved; but as a rule the spherical sac was rather sharply demarcated at the junction of the cystic and hepatic ducts. The hepatic branches were usually dilated, but in none of the cases did they form a part of the actual cyst. There was frequently a definite line or fold at the junction of the hepatic duct or its branches with the cyst.

The terminal duodenal nondilated portion of the choledochus: The terminal portion of the choledochus is never involved in the cystic dilatation and usually joins the dilated globular sac at an acute angle. It consists of an intraduodenal portion and usually of an extraduodenal part, which only in some cases was found surrounded by pancreatic tissue. The lumen was found obliterated in only one case (Lavenson). Here the extraduodenal portion was 1 cm. long, cordlike and patulous, but the intramural part, which was 2 cm. long, was obliterated, with an absence of epithelium.

In fourteen cases, a patent lumen was either not demonstrated or not mentioned. In three of these cases, the necropsy report was incomplete (Cases 8, 25, 27). In one case, a necropsy was not obtained (Case 38). In Weiss' case, it was impossible to pass a sound from the papilla into the cyst, and the specimen was destroyed, preventing further search. Ashby [26] found no opening on examination. There may have been obliteration of the lumen since there had been continuous jaundice for two years. In the remaining eight of these cases, the only search for the duct was the one made at the operation. In two of these, it is possible that obliteration of the duct may have occurred, since there was a history of continuous jaundice for two years and three months, respectively (Cases 40, 43). In two (Cases 35, 47), there was never more than a slight trace of icterus, and in the remaining four (Cases 44, 37, 46, 48), it is apparent from the symptoms that complete obliteration of the duct did not occur.

---

26. Ashby, H.: Med. Chron. **10**:28 (Oct.) 1898.

In thirty-three cases, a lumen was reported present in the terminal choledochus from the cyst into the duodenum. In one of these, it was found only after serial sections were made for microscopic examination (Case 17).

A narrowing of the lumen was described in eleven cases (Cases 28, 9, 16, 4, 1, 39, 7, 2, 17, 5, 31).

A valve formation was described at the junction of the cyst and the terminal duct in sixteen cases (Cases 1, 2, 12, 11, 23, 16, 26, 32, 18, 21, 42, 34, 45, 6, 5, 10). Seyffert, Wettwer and Fenger state that this valve action completely prevented the contents of the cyst from entering the duodenum, even after compression of the cyst.

There was a sharp kink or angle, which in some cases was S-shaped, described in ten cases (Cases 17, 20, 2 3, 5, 10, 36, 15, 7, 31). In some cases, all three of these conditions existed.

In the remaining six of the thirty-three cases with a patent lumen, the authors state that there was found no apparent cause for the obstruction of the terminal duct (Cases 41, 29, 30, 33, 14, 19).

Length and course of the nondilated choledochus: In Seyffert's case, the terminal duct was 5 cm. long. In Konitzky's case, it was 2.5 cm. long. The upper end entered the cyst on its lower left wall and passed through the wall obliquely from behind forward. The lower end entered the duodenum 4 cm. below the pancreatic duct and its normal location. The duct was 2.7 cm. long in Heid's case. In Rostowzew's case, it was 3 cm. long and went obliquely through the duodenal wall from the right above to the left below. In Dreesmann's case, it was 3 cm. long and passed obliquely through the wall downward and to the right. In Wettwer's case, the duct was 2 cm. long. In Wagner's case, it was 3 cm. long, passed through the head of the pancreas and entered the duodenum normally from left to right. In Robert's case, the duct was 1 cm. long. In Waller's case, the duct passed out of the lower pole of the cyst to the left and was from 3 to 4 cm. long. In Budde's case, the duct measured 1 cm. to the junction with the ductus pancreaticus. The diverticulum of Vater was large and measured 4.5 cm. long. Schloessmann[27] described a pea sized dilatation in the narrow duct between the cyst and its point of union with the pancreatic duct. In Heiliger's case, there were several fine openings in the bile papilla, which opened 9 mm. below the pancreatic duct. In Kolb's case, the bile duct emptied separately from the pancreatic duct.

The cystic duct: This was described as normal seven times (Cases 19, 47, 29, 38, 30, 33, 11). In Rostowzew's case, however, there was a

27. Schloessmann: Beitrag zur Kenntnis der Choledochuscysten, Deutsch. Ztschr. f. Chir. **109**:161, 1911.

valvelike formation above. The duct was obliterated in Edgeworth's case; slightly narrowed and with a kink in Roberts' and compressed in Lavenson's. Schurholz [28] described it as shrunken.

The cystic duct was dilated in nineteen cases (Cases 5, 6, 7, 16, 15, 18, 20, 21, 14, 13, 12, 48, 3, 34, 39, 23, 10, 32, 44). In Fenger's case, there was also a valve compressive action at the neck of the gallbladder. There was a dilatation of only the lower one half of the cystic duct in four cases (Cases 1, 2, 17, 4). The cystic duct was not described in fourteen cases (Cases 8, 28, 27, 26, 25, 24, 35, 37, 46, 45, 43, 42, 40, 41).

Gallbladder: The size was described as normal in sixteen cases (Cases 1, 2, 3, 4, 6, 11, 14, 17, 19, 21, 32, 36, 38, 40, 42, 45). It was dilated in seventeen (Cases 5, 7, 22, 44, 23, 28, 30, 33, 13, 15, 18, 20, 10, 34, 39, 43, 12). In Russell's case, it was extremely dilated.

The gallbladder was small in seven cases (Cases 9, 29, 47, 31, 48, 46, 24). In Roberts' case, it contained clear mucus; it was atrophic in two cases (Cases 46, 24), and it was not described in eight cases (Cases 25, 26, 27, 8, 16, 35, 37, 41).

There were papillomatous areas covered with cylindrical epithelium, some ulcers, necrosis at the fundus of the gallbladder, and areas of round-cell infiltration resembling abscess formation in the tunica fibrosa in Wagner's case. Rotgans [29] found the wall of the dilated gallbladder from 4 to 6 mm. thick.

There was a palpable gallbladder as a second tumor outlined through the abdominal wall in five cases (Cases 12, 30, 15, 20, 18).

The hepatic ducts were described as dilated in thirty cases (Cases 19, 1, 31, 5, 48, 2, 11, 10, 36, 4, 6, 3, 9, 12, 14, 7, 24, 15, 16, 18, 21, 28, 30, 23, 22, 33, 34, 39, 40, 42). There was a finger-sized dilatation described in five (Cases 19, 1, 31, 11, 48). In Douglas' case, the dilatation of the hepatic ducts only extended to the second and third branching. In Heid's case, the dilatation of the intrahepatic ducts extended only about 4 cm. In Rostowzew's case, the dilated hepatic duct met the sac tangentially. The right hepatic branch had a crescent shaped valve, and also the cystic; but the left hepatic branch opened directly into the sac. In two, the hepatic ducts were described as normal (Cases 47, 17). In sixteen no mention was made of the condition of the hepatic ducts (Cases 8, 13, 20, 25, 26, 27, 29, 32, 38, 35, 37, 46, 45, 43, 41, 44). There were crescentic folds or valve formations at the junction of the hepatic ducts and the sac in five

28. Schurholz: Ein Fall sog. idiopathischer Choledochuscyste, Arch. f. klin. Chir. **118**:91, 1921.

29. Rotgans: Aangeboren choledochus afwijking, Nederl. Tijdschr. v. Geneesk. **49**:1345 (Oct. 11) 1913.

cases (Cases 32, 17, 23, 34, 40). In three, the openings of the cystic duct and the two hepatic branches into the sac all had valvelike formations (Cases 32, 23, 34).

The liver: This was not described in thirteen cases (Cases 1, 8, 16, 19, 21, 23, 25, 27, 29, 32, 40, 41, 46). In twelve, the liver was described as normal (Cases 15, 14, 12, 4, 30, 47, 3, 38, 42, 43, 45, 37). In one, microscopic examination was described as normal (Case 37).

In five cases, an enlarged liver was described, without its being characterized as a cirrhosis or a hepatitis (Cases 10, 44, 2, 6, 18). In Heid's case, it was markedly enlarged; in Seyffert's case, it was also icteric, and in Arnold's case, it was enlarged and nodular, owing to the swollen small liver lobules.

In one, the liver was simply described as icteric (Case 28).

In three, it was described as of some grade or type of hepatitis, but not cirrhotic (Cases 33, 39, 48). In Wagner's case, the liver was enlarged. There was purulent bile in the ducts. On microscopic examination, there was a parenchymatous hepatitis with cell degeneration.

Zipf [30] described hepatic swelling with evidence of chronic and acute inflammation, and multiple necrotic areas in the liver.

There was a cirrhosis of the liver described in fourteen cases. In nine of them, there was said to be a characteristic biliary cirrhosis (Cases 13, 22, 11, 36, 31, 9, 20, 35, 34). Clairemont [31] described only a slight interstitial hepatitis microscopically.

In Weiss' case, the liver was enlarged. Microscopically, it showed inflammation with marked connective tissue increase and pressure destruction of the liver strands by the connective tissue about the acini, but no changes in the blood vessels or the bile capillaries.

In Kolb's case in which the terminal duct could be found only in serial sections, the huge liver reached to the ileum, and the spleen was also enlarged. The liver appeared cirrhotic. Microscopically, there was an interstitial hepatitis, with increased connective tissue, some round cells in the acini, newly formed blood vessels and bile capillaries.

In Wettwer's case, there was an enlarged icteric liver with increased periportal connective tissue. There was enlargement of the spleen. Here, there was a terminal diffuse tuberculous peritonitis.

In Konitzky's case, the enlarged liver was icteric, and there was an interstitial hepatitis observed on microscopic examination.

---

30. Zipf, K.: Ueber diopathische Choledochuscysten, Arch. f. klin. Chir. **122**:615 (Jan. 27) 1923.

31. Clairemont: Diskussion zur typischen Erweiterung des Choledochus, Wien. klin. Wchnschr. **24**:1616, 1911.

In contrast to the inconstancy of biliary cirrhosis of the liver in this group of cases with incomplete, intermittent obstruction, Beneke,[32] in a review of cases of congenital obliteration with complete obstruction of the choledochus, found that there existed a pronounced cirrhosis of the liver in all cases. He stated that the intrahepatic bile ducts are atrophied and sometimes there is no trace of them, and that definitive occlusion either during embryonal development, or after ligation of the choledochus experimentally, forces the bile into the blood; the canaliculi are superfluous, and the liver is transformed into a gland of internal secretion. The extrahepatic bile ducts are not dilated as a rule in congenital obliteration of the choledochus. There are two exceptions, the cases of Wickham-Legge and Oxley.

Mayo Robson stated that cirrhosis of the liver is rarely found with obstruction of the bile ducts in adults, and when present is associated with stones and infection; but it is constant with congenital obliteration of the ducts.

The cyst wall: This was usually dark, and in many cases was covered by adhesions and blood vessels. It was usually described as tough and thick. It is described as being from 1 to 5 mm. in thickness and as having lost its bile duct structure. Ulcerations were present on the inner wall in the cases of Seyffert and Dreesmann. There were encrustations in Arnold's case. In Waller's case, the wall was very friable and the terminal duct tore away from its junction with the sac while it was being examined.

The microscopic examination was reported in only twenty-four cases. Bolle [33] described the sac wall as resulting from chronic inflammation of a changed bile duct. In twenty of the remaining twenty-three cases, there was stated to be an entire absence of epithelium on the cyst wall (Cases 5, 17, 9, 11, 19, 20, 21, 22, 24, 36, 7, 26, 29, 30, 33, 31, 34, 43, 47, 48). Zipf, Seyffert and Reel and Burrell [34] were the only writers who described an epithelial layer on the inner wall of the cyst.

In nine of the twenty-three cases, the fibrous wall was reported as being without any differentiated structure, as epithelium, muscle or elastic tissue (Cases 9, 22, 24, 26, 7, 19, 31, 47, 43). Ebner reported an absence of epithelium, without further description. In addition to the fibrous tissue, Mayesima [35] describes numerous elastic fibers. Muscle fibers were also present in seven cases (Cases 5, 17, 33, 39, 30, 26, 34).

---

32. Beneke: Program, Marburg, 1907; quoted by Roberts.

33. Bolle, H.: Ein Fall von idiopathischer Choledochuscyste, Deutsch. med. Wchnschr. **48**:1381 (Oct. 13) 1922.

34. Reel, P. J., and Burrell, N. E.: Cystic Dilatation of the Common Bile Duct, Ann. Surg. **75**:191 (Feb.) 1922.

35. Mayesima, J.: Zur Kasuistik der primären cystischen Erweiterung des Ductus choledochus, Deutsch. Ztschr. f. Chir. **119**:338, 1912.

In many cases, there were three zones to be made out, an inner zone of quite compressed fibers, a middle one of moderately loose fibrous tissue and an outer one of loose connective tissue and numerous blood vessels.

Budde described a few glands in the outer fibrous layer resembling undeveloped mammary acini, which were somewhat flattened and were covered with cuboid or cylindrical epithelium.

Rostowzew and Reel and Burrell also described occasional cross-sections of small openings lined with a single layer of columnar cells, closely resembling the structure of the smaller bile ducts found within the liver.

Seyffert stated that the cyst wall was covered by cylindrical epithelium, except the lower part, which was ulcerated.

There was some round-cell infiltration present in the fibrous wall in a few cases (Cases 29, 30, 36, 31).

Zipf described chronic inflammation of a thickened choledochus wall. The layer of cylindrical epithelial cells was in bad condition. There were a few tubulo-alveolar glands in the tunica propria.

Ascites, with evidence of pressure on the portal vein by the cyst, was present in five cases (Cases 5, 2, 13, 20, 34). There was edema of the legs in three cases (Cases 13, 1, 34). There was evidence of pressure of the cyst on the superior mesenteric vessels, with compression of the underlying duodenum in three (Cases 30, 43, 47). There was retroflexion of the uterus and pressure by the cyst in Seyffert's case.

Pregnancy occurred in five cases (Cases 6, 15, 43, 19, 48). In the case of Goldammer, there was noticed a swelling of the abdomen under the right costal arch directly after delivery, and jaundice appeared within a week.

In Dreesmann's case, the symptoms began during infancy and recurred from time to time. The patient had a normal pregnancy; but two months after delivery, she had a recurrence of the symptoms, so severe that she went to the hospital.

Hildebrand [36] stated that the onset of acute attacks occurred at the seventh month of pregnancy. Artificial labor was induced and one or two days after a normal delivery, jaundice appeared. Other symptoms followed, with emaciation, and three months later, she entered the hospital. Four years after operative cure, she gave birth to a normal child. In Seyffert's case, the onset with jaundice began after childbirth. With the exception of four months, this was constant for two years, with the development of a tumor and acute colic.

An associated mental defective condition was present in two cases (Cases 35, 47).

---

36. Hildebrand: Geheilte Choledochuscyste, Deutsch. med. Wchnschr. **39**: 2224, 1913.

In Heiliger's case, there was a diaphragmatic hernia on the left side, consisting of almost the entire abdominal organs and intestines.

Symptoms.—The characteristic symptoms were recurrent attacks of jaundice, abdominal pain in the region of the liver and a palpable cystic tumor developing during childhood or youth, as shown in the accompanying table.

The onset was acute, with only a few days' duration in six cases: five days (Case 12), four days (Case 30), three days (Case 39), one week (Case 31) and two and one-half weeks (Case 23). The onset was acute in Wagner's case, two weeks before, but there had been a slight abdominal pain for a year.

The symptoms were of a longer duration in the others: a few weeks (Case 38), six weeks (Cases 28, 36), two months (Cases 46, 17), three months (Cases 42, 19, 7, 2), four months (Cases 29, 43), six months (Case 27), ten months (Case 20), one year (Cases 14, 22, 35), fourteen months (Case 24), eighteen months (Case 3), two years (Cases 6, 18, 40, 47), two and one-half years (Case 16), three years (Cases 1, 13, 11, 41, 45), four years (Cases 9, 44, 42), nine years (Cases 34, 21), ten years (Case 5), twenty-three years (Case 15), twenty-five years (Case 10), thirty-six years (Case 37), forty-nine years (Case 48). The duration was not mentioned in three cases (Cases 8, 25, 26).

In Heiliger's case, the infant, which was almost full-term, was born dead.

The onset of symptoms occurred at the age of 6 months in four cases, and in more than 50 per cent., the symptoms developed when the patient was under 10 years of age.

The sex was: female, forty-one cases; male, six (Cases 24, 25, 26, 12, 20, 4). The sex was not stated in Arnison's case.

Jaundice was the first symptom in thirteen cases (Cases 6, 42, 48, 22, 27, 3, 11, 13, 14, 15, 16, 18, 19). Colic or abdominal pain was the first symptom in eight cases (Cases 31, 45, 35, 47, 30, 33, 34, 21). Abdominal swelling was the first symptom noted in four cases (Cases 17, 37, 9, 20). There were all three symptoms at the onset in eight cases (Cases 1, 7, 46, 23, 36, 38, 39, 12). Pain and swelling were both noted at the onset in six cases (Cases 2, 5, 32, 28, 41, 43). Jaundice and pain were noted together at the onset in three cases (Cases 10, 24, 44). Jaundice and swelling began together in two cases (Cases 40, 29). Onset of symptoms was not stated in three cases (Cases 25, 8, 26). The remaining case was congenital (Case 4).

Jaundice was the most constant symptom. It was absent in Heiliger's congenital case and in two others (Cases 32, 41). No symptoms were mentioned in the case of Arnison.

The jaundice was continuous from its onset in thirteen cases. (Cases 12, 16, 20, 40, 42, 43, 36, 22, 23, 19, 33, 7, 17). In ten of these, a patent lumen was demonstrated in the terminal bile duct. However, it was found only on serial sections, and was very small in the case of Kolb. In two of these, the outlet was not seen (Cases 40, 43). In only one case was the intramural part of the duct obliterated (Case 22). The duration of the jaundice was less than three months in ten of these. Swain [37] stated that it was continuous for two years. In Lavenson's case, it persisted one year, and in the Guy's Hospital case for two and one-half years. Acholic or white stools were stated to be present in nine of the cases, with continuous jaundice. In the other four cases, it was not mentioned (Cases 12, 16, 20, 19).

It was not stated in eight cases whether the jaundice was continuous or not (Cases 25, 26, 27, 29, 34, 47, 18, 21). In five of these, the presence of acholic stools was not mentioned. In one case, acholic stools were never present (Case 34). In the others, acholic stools were present (Cases 47, 21).

Jaundice was intermittent in twenty-three cases (Cases 13, 24, 28, 38, 39, 10, 48, 46, 37, 9, 11, 6, 14, 15, 3, 5, 1, 2, 31, 44, 47, 45, 35). Acholic stools were observed in fifteen of the twenty-three cases of intermittent jaundice. Whether it was observed was not stated in two cases (Cases 37, 11). There were no acholic stools in six cases (Cases 24, 39, 9, 45, 35, 31).

Tumor and abdominal pain in the region of the liver were, after jaundice, the most characteristic symptoms. The onset of these two symptoms occurred at the same time, previous to examination, in thirteen cases (Cases 39, 14, 23, 28, 36, 46, 2, 19, 43, 1, 41, 32, 5).

In eleven other cases, the onset of pain and tumor was noted at different times (Cases 12, 35, 47, 24, 37, 6, 30, 15, 34, 21, 11). In four cases, the time of onset was not stated (Cases 33, 45, 38, 26).

In nine cases, there was said to be an entire absence of pain, but in these cases the tumor was present (Cases 7, 17, 40, 22, 29, 3, 42, 16, 31). In seven cases, pain was not mentioned as a symptom, but a tumor was complained of (Cases 20, 9, 18, 25, 8, 13, 27).

However, in the three cases in which a tumor was not noticed, pain was present (Cases 44, 10, 48). The remaining case was congenital (Case 4). In the majority of the cases, the pain was severe and colicky in character during the attacks, and in some cases it recurred with each meal or after any indiscretion in diet. It was said to be only a slight distress in a few cases (Cases 11, 19, 33).

37. Swain, W. P.: A Case of Cholecystenterostomy with the Use of Murphy's Button, Lancet **1**:743, 1895.

Summary of Cases *

Case	Year	Age at Entrance, Years	Treatment	Results
			Cases Without Operation	
1. Douglas†	1852	17	Aspiration	Death 14 days later
2. Held [18]	1893	14	Medical	Death 4 months later of erysipelas and diphtheria
3. Broca ‡	1897	10	For tuberculosis	Death from generalized tuberculosis
4. Heiliger [7]	1905	0	Stillbirth	Congenital
5. Wettwer [17]	1905	15	Medical	Death from miliary tuberculosis
			Operation Without Recovery	
6. Seyffert [19]	1887	23	Drainage	Death 1 month later from anemia following hemorrhage
7. Konitzky [16]	1888	21	Drainage	Death 8 days later from weakness
8. Arnison [3]	1891	?	Drainage	Death 1 day later
9. Edgeworth [15]	1895	4	Drainage	Death 1 week later, cardiac failure
10. Fenger [21]	1896	33	Drainage of gallbladder	Death 1 day later, weakness
11. Rostowzew [13]	1897	13	Drainage	Death 1 day later
12. Russell [23]	1897	8	Drainage	Death 4 days later from hemorrhage
13. Ashby [26]	1898	7	Ten aspirations; drainage operation; a later operation with attempt at anastomosis between cyst and duodenum	Death 1 day later from peritonitis
14. Nicolaysen §	1899	8	Drainage	Death 1 day later
15. Dreesmann [8]	1904	24	Drainage; 4½ months later, operation with anastomosis between cyst and duodenum with Murphy button	Death 3 days later
16. Guy's Hosp. Case Spec. No. 1419; Moynihan ¶	1904	21	Two aspirations; drainage operation	Death 2 days later
17. Kolb [12]	1905	10	Aspiration; drainage a few days later	Death 1 month later
18. Arnolds [25]	1906	13	Drainage	Death 1 day later from hemorrhage
19. Goldammer [11]	1906	21	Extirpation of cyst and drainage	Death a few hours later from hemorrhage
20. Mayesima [25]	1907	2	Aspiration; operation, incision of sac and closure	Death 2 months later
21. Ebner [9]	1908	18	Drainage	Death 3 months later from purpura hemorrhagica fulminans
22. Lavenson [4]	1909	8	Extirpation of cyst and drainage of gallbladder	Death 1 month later from hemorrhage
23. Schloessmann [27]	1909	7	Aspiration followed by drainage	Death 6 days later from peritonitis, due to bile leak from aspiration
24. Weiss [10]	1909	6	Aspiration, followed by drainage operation 1 day later	Death 9 days later from exhaustion; peritonitis after aspiration
25. Butters #	1910	5	Drainage	Death few days later from exhaustion
26. Clairemont [21]	1911	22	Drainage	Fistula; death 3 years later from pulmonary tuberculosis
27. Exner ‖	1911	23	Drainage	Death few days later of hepatic insufficiency

* The case numbers in the text refer to the cases in the table. The data are included in the text so that a complete table of symptoms and pathologic conditions can be reconstructed.

† Douglas, A. H.: Case of Dilatation of the Common Bile Duct, Monthly J. M. Sc. (London) **14**: 97, 1852.

‡ Broca: Dilatation énorme du canal choledoque, Bull. Soc. de chir. de Paris **25**: 209 (March 10) 1897.

§ Nicolaysen, J.: Tumor cysticus ductus hepatici et choledochi dilatati, Nord. med. Ark. **16**: 1 (Aug.) 1899; Centralbl. f. Chir. **26**: 1264, 1899.

¶ Moynihan, B. G. A.: Brit. M. J. **2**: 1391 (Nov. 25) 1905; Gallstones and Their Surgical Treatment, Philadelphia, W. B. Saunders Company, 1904, p. 81.

Butters: Choledochuscysten, Deutsch. med. Wchnschr. **36**: 1351, 1910.

‖ Exner, A.: Wein. klin. Wchnschr. **24**: 1615 (Nov. 10) 1911.

Summary of Cases—(Continued)

Case	Year	Age at Entrance, Years	Treatment	Results
28. Ipsen **	1913	18	Drainage of cyst and gall-bladder	Death 1 month later of hemorrhage
29. Letulle ††	1913	25	Drainage	Death 8 days later of hemorrhage
30. Seeliger [14]	1913	13	Drainage; 2 weeks later anastomosis between cyst and duodenum with rubber tube	Death 8 days afterwards
31. Roberts [22]	1914	2	Drainage	Death 1 week later, weakness
32. Smit [1]	1915	17	Extirpation of cyst and ligation of bile ducts	Death 8 days later
33. Wagner [24]	1918	47	Anastomosis between cyst and duodenum with Murphy button; cholecystectomy	Death 4 days later from cholangitis, preexisting
34. Budde [20]	1920	22	Drainage	Death 1 day later from weakness
35. McConnell ‡‡	1920	11	Drainage; 8 months later, drainage again of sac for infection; 3 years later, exploration of cyst; closed	Occasional attacks of pain continuing until 8 months after last operation
36. Schurholz [28]	1921	3	Aspiration; 1 day later drainage; 3½ months later, attempt to anastomose cyst and duodenum	Death 3 hours later from cardiac weakness
37. Reel and Burrell[34]	1922	50	Drainage; 3 weeks later, drainage of abscess	Fistula for 9 months; 1½ years later, patient in good health
38. Ashby-Platt (Morley, J.)§§	1923	6	Drainage; 2 months later, attempt to close bile fistula	Death a few hours later
39. Zipf [30]	1923	14	Drainage	Death 3 days later from preexisting cholangitis
			Operation With Recovery	
40. Swain [37]	1894	17	Aspiration; choledochojejunostomy with a Murphy button	Cured
41. Brun-Hartmann ¶¶ (Veau, U.)##	1897	3½	Drainage; choledocho-enterostomy at a second operation	Cured
42. Bakes [5] (Sternberg)	1907	22	Choledochduodenostomy	Cured; death 4 years later from other causes (Sternberg)
43. Hildebrand [36]	1912	18	Drainage; choledochoduodenostomy at a second operation; a larger choledochoduodenostomy stoma at a third operation	Cured; observation 6 years later (Kremer)[43]
44. Rotgans [29]	1913	5	Drainage and cholecystectomy; 4 months later, a choledochoduodenostomy, with a small stoma	Probably cured; observation 1 year later; a few slight attacks
45. Waller [6]	1916	10	Choledochoduodenostomy	Cured; observation 10 months later
46. Bolle [33]	1922	13	Aspiration; drainage a few days later; choledochoduodenostomy, closure of fistula and cystectomy 2 weeks later	Cured; observation 2 years later
47. Morley (Compare Case 38)	1923	17	Drainage; choledochoduodenostomy 3 weeks later and closure	Cured; observation 1 year
48. McWhorter	1922	49	Cholecystostomy 14 years before; no relief; hepaticoduodenostomy, with excision of sac and cholecystectomy	Cured; observation 1 year later

** Ipsen, J.: Et Tilfaelde af Choledochuscyste, Hospitalstidende **45**: 1342, 1913.
†† Petulle, M.: Dilatation kystique des voies biliaires, Presse méd. **21**: 97, 1913.
‡‡ McConnell, A. A.: Cyst of the Common Bile Duct, Brit. J. Surg. **7**: 520 (April) 1920.
§§ Morley, J.: Congenital Cyst of the Common Bile Duct, with Report of Two Cases, Brit. J. Surg. **10**: 413 (Jan.) 1923.
¶¶ Brun-Hartmann: Bull. Soc. de chir. de Paris **23**: 207 (March 10) 1897.
Veau, U.: Retrecessements congenitoux des voies biliaires et leur traitement chirurgical, Presse méd. **52**: 475, 1910.

Fever, usually of moderate degree, was complained of during the attack in eighteen cases (Cases 33, 30, 29, 5, 23, 36, 39, 41, 45, 46, 31, 20, 15, 14, 12, 1, 11, 48). There was evidence of inflammation of the bile ducts or liver in six of these, and here the fever was high (Cases 33, 29, 15, 1, 36, 39). In two, bacteria were cultured (Cases 36, 39). Fever was said to be absent in ten cases (Cases 28, 47, 43, 42, 24, 7, 44, 2, 17, 19). Fever was not complained of in the remaining twenty-five cases. In twenty of these in which there was evidence obtained at operation or necropsy, it showed an absence of acute or pyogenic inflammation.

Diagnosis.—The correct diagnosis was not made in any case before operation. The most common error made was in diagnosing the condition as echinococcus cyst of the liver, in fourteen cases. Other diagnoses were pancreatic cyst, hydronephrosis, obstruction of the common bile duct, dilated gallbladder, retroperitoneal cyst, ovarian cyst, advanced pregnancy, cholelithiasis (Case 44), cyst of the kidney, chronic peritonitis (Case 34) and generalized tuberculosis (Case 3).

The diagnosis was not made at the exploratory operation in practically all of the cases that resulted fatally.

Prognosis and Operative Treatment.—The condition is apparently a progressive one. Consequently, operation should be performed while the patient is still in good condition. The high death rate was partly due to the fact that many of the patients were badly jaundiced and emaciated. Exploratory operation alone or combined with external drainage has resulted almost invariably in the death of the patient. The prognosis, then, depends not only on early operation but also in establishing adequate intestinal drainage. A serious factor in two patients that died was leakage of bile following an exploratory aspiration, with evidence of peritonitis (Cases 23, 24). Aspirations performed on eight others resulted in no bad effects. All of the patients that underwent drainage externally without a later operation with intestinal drainage died, with two exceptions (Cases 35, 37). Thirty deaths may be classed as operative; from the disease, from operative shock and from loss of strength and emaciation due to the external drainage. Ebner's patient died three months after operation from purpura hemorrhagica fulminans, and Clairemont's patient died three years later, with persistent biliary fistula. McConnell's patient was operated on a second time in an effort to overcome the attacks of pain, although nothing was done at the operation, since the cyst had shrunk in size. However, there were still attacks of pain during the next eight months of observation. Reel and Burrell's patient was alive and without symptoms, but there was a biliary fistula for nine months, and since postoperative observation was reported for only one and one-half years, it is not included as a case of cure.

There was a low mortality only in the cases in which drainage was established into the intestine at the first operation. However, the opening must be adequate or contraction and a recurrence of the obstruction may result, requiring another operation, as in Hildebrand's case. In Rotgan's case in which a small stoma was made, there was a recurrence of a few slight attacks of pain during one year of observation. The nine patients that may be classed as cured all eventually had a permanent stoma made between the bile duct and the intestine. A duodenal anastomosis with partial or complete excision of the sac, when conditions are favorable, would reduce the stasis of bile with intestinal contents and, I believe, lessen the tendency to a cholangitis. Fowler believed excision of the sac would have avoided the infection and cholangitis that resulted from duodenal drainage of a retention cyst of the common bile duct in a somewhat similar case. Mayo Robson [38] stated that extreme dilatation of the biliary passages is often accompanied by infection.

In twenty-two cases, external drainage alone was established. All the patients died without complete recovery. In two cases, external drainage was performed, but a second operation was necessary, in one for drainage of the infected sac and in the other for an abscess (Cases 35, 37). In ten cases, external drainage was done at the first operation, and a choledochoenterostomy was performed at a later operation. Five of these patients recovered (Cases 47, 41, 46, 44 and Hildebrand's). The other patients died (Cases 15, 30, 36, 13, 38). In two cases (Cases 15, 38), it is not clear whether the anastomosis was successfully completed. In four cases, there was a primary choledochoenterostomy performed with three recoveries (Cases 45, 42, 40). In the other (Case 33), death was due to a preexisting cholangitis. Three patients (Cases 19, 22, 32) died following excision of the sac without intestinal drainage, but in one the hepatic duct was ligated. In one fatal case (Case 20), there was an incision and closure of the sac without drainage.

The surgical indication, it seems, is to perform a primary drainage of the bile ducts into the adjacent duodenum, stomach or intestine, and, if conditions are favorable, complete or partial excision of the sac.

38. Mayo-Robson: Lancet **1**:1529-1671 (June) 1897.

A CLINICAL STUDY OF THE MOBILITY OF THE HUMAN SPINE

ITS EXTENT AND ITS CLINICAL IMPORTANCE *

HENRY KELLER, M.D.

NEW YORK

In order thoroughly to understand the mobility of the human spine, it is advisable to subdivide the subject matter to be discussed into its respective component parts: 1. The anatomy and the physiology of the spinal column. 2. The mechanics and dynamics. 3. The foramina for the nerve exits and the connective links between the cerebrospinal and the sympathetic nervous system. 4. The mobility of the spine, with the proofs of this mobility. 5. The clinical application of this knowledge.

ANATOMY OF THE SPINE

The spinal column is made up of a series of separate bone segments called vertebrae, thirty-three in number, divided into seven cervical, twelve dorsal, five lumbar, five sacral and four coccygeal. In adult life, with the exception of rare cases, the parts making up the sacral portion are fused, forming one bone, called the sacrum, and the four coccygeal bones make up the coccyx. The vertebrae are placed one upon another, thus forming a strong supporting pillar or column. Throughout the length of this column runs a hollow cylindrical canal, which contains and protects the spinal cord.

Between the vertebrae of human beings are found pads of tough, resilient fibrocartilage, called intervertebral cartilages or disks. These intervertebral disks, which are like pieces of India rubber, act as shock absorbers or buffers, and at the same time permit of movement between the vertebrae. In the intervertebral joints, movement is permitted only to the extent of the flexibility of the rubber-like intervertebral disks.

A disk is composed of fibrocartilage at its periphery, and a soft pulpy substance in the center. The fibrous tissue and fibrocartilage are arranged in concentric rings. These rings are not absolutely cylindrical, nor are they at exactly right angles to the adjacent vertebrae, but they bulge out from the pulpy mass in the center, which is under pressure.

The structure of the disk is admirably adapted to minimize jarring of the vertebrae and at the same time allow a degree of relative sliding movement between them. Hence, in the cervical and lumbar regions, where the intervertebral disks are the thickest, the movements are freest.

---

* From the orthopedic department of the University and Bellevue Medical College.

Component Parts of the Vertebrae.—Each vertebra is composed of two essential parts: (*a*) a body in front and (*b*) a neural arch behind.

(*a*) Bodies of the vertebrae are composed of spongy bone. They are more or less oval, flattened from above downward, and are narrower in the middle than at the edges. The internal architectural arrangement of the lamellae of bone comprising the body of the vertebrae is such that the principal lamellae lie in a plain parallel to that of the line of greatest stress. The upper and lower surfaces are slightly concave for the reception of the intervertebral disks, and roughened at the edges for the attachment of ligaments.

(*b*) Each neural arch springs from its corresponding body by two legs or pedicles. These are short flattened bony processes, and with two other flattened bony processes go to complete the arch. At the junction of the pedicles and laminae, the articular processes are situated, for articulation with the vertebrae above and below. At the junction of the laminae is the spinous process, a rough thickened process of bone which affords attachments for muscles and ligaments.

Each neural arch is joined to the arch of the vertebra above and below by ligaments consisting of yellow elastic tissue, and so a hollow cylinder or tunnel is formed for the transmission of the spinal cord, permitting movement of the spine, while protecting the enclosed spinal cord. The articular processes which spring from about the junction of the pedicles and laminae serve the double purpose of allowing movement and at the same time interlocking the bones. Sir George Humphry is quoted by Gray as having pointed out that the movements permitted in the spine are mainly due to the shape and position of the articulating processes. Thus, in the loins, the inferior articulating processes are turned upward and embraced by the superior, which renders rotation in this region of the spine impossible; while there is nothing to prevent a sliding upward and downward of the surfaces on each other, to allow flexion and extension. In the dorsal region, the articulating processes, by their direction and mutual adaptation, especially at the upper part of the series, permit rotation, but prevent extension and flexion; while in the cervical region, the greater obliquity and lateral slant of the articular processes allow not only flexion and extension, but also rotation.[1]

Between the adjacent vertebrae on either side are found oval openings called intervertebral foramina. The foramina communicate with the spinal canal, and each contains the spinal nerves, which are composed of motor and sensory fibers, carrying afferent and efferent impulses to and from the cord; a few small arteries, which carry nourishment to the corresponding segments of the spinal cord; a few small veins and

1. Gray's Anatomy, American Edition, Philadelphia, Lea Bros. & Co., 1897, p. 323.

lymph vessels, which drain waste products from the spinal segments, and a small amount of fibrous connective tissue, which surrounds all these structures and forms a cobweb-like structure, the meshes of which contain semifluid, compressible fat tissue in abundance, filling all space not occupied by the other structures.

Spinal Curves.—At birth, the spinal column is, more or less, a curved chain of bones, with its convexity directed backward. As age advances and the child begins to hold up its head, the intervertebral disks grow in such a manner that a curve is developed in the cervical region with its convexity directed forward. As the child sits up and begins to walk, a curve is developed in the same way in the lumbar region of the spine, with its convexity forward. The intervertebral disks thus become much thicker in front than behind in the cervical and lumbar regions, while they remain uniformly thick in the dorsal region. The intervertebral disks form about one fourth of the spinal column, exclusive of the first two vertebrae; but they are not equally distributed between the various bones, the dorsal portion of the spine having, in proportion to its length, a much smaller quantity than the cervical and lumbar regions. The movements of the spine, occurring as they do through the medium of the intervertebral disks, are naturally most free in the cervical and lumbar regions. The intervertebral disks in the dorsal region do not alter the curve of the region, and so this is called a fixed curve. It is really more or less fixed as far as anteroposterior movement of the spine is concerned.[2]

Importance of the Spinal Curves.—The importance of the spinal curves is better understood when one takes the trouble to compare the human skeleton with skeletons of back-boned animals, in all of which the spine comprises the central sustaining shaft which supports all the rest of the framework. The skull is attached to the front, the ribs and forelimbs to the sides, the hip bones, hind limbs and tail to the rear, while the animal walks on all fours. The suspension of the spine in a horizontal position facilitates the interlocking of the articular processes of the vertebrae. The human spine, because it performs its function in the erect posture, is at a constant disadvantage, this position not only preventing the proper interlocking of the vertebrae, but also bringing the weight of the head and chest outside the center line of the body. To overcome this difficulty, the various curves of the spine gradually develop, in order to maintain the line of gravity; the muscles of the back helping to maintain the position.

The presence of the curves also adds to the resiliency of the spinal column, as pointed out by McKendrick; for if the spine were straight,

2. McKendrick, A.: Back Injuries and Their Significance Under the Workmen's Compensation and Other Acts, New York, William Wood & Co., 1916.

and the vertebrae were not separated from one another by intervertebral disks, the jar from every step would be transmitted directly to the head.[3]

After adult life, and as age advances, the intervertebral disks gradually become more and more fibrous, and tend to disappear. The spine gradually loses its lumbar curve, and to some extent its cervical curve, and slowly and gradually reverts to its original curve with its convexity backward. The center of gravity being thus altered, the old man must stand with his knees and hips bent, in order to maintain his balance.

Spinal Curves and Roentgen-Ray Examinations.—It is important to remember the natural law that roentgen rays, like light rays, travel in straight lines; also that the roentgenogram is a shadow picture, and hence the further the opaque object is removed from the screen on which it falls, the larger will be its shadow, and the less distinct its outline. McKendrick pointed out further that the rays are able to, and actually do, penetrate solid objects, and therefore cast a shadow of the near as well as the far side of the object. The roentgen-ray shadow of any wedge-shaped object is accordingly misleading. These facts must be borne in mind when roentgenograms of the spinal column are interpreted.

Because of the normal curves of the spinal column, it is essential to recall that, if a large surface is covered, some vertebrae will throw a more distinct shadow on the plate than others, owing to their nearness to the sensitive plate. The shape of the vertebrae in question must also be taken into account. The body of the fifth lumbar vertebra is far removed from the roentgen-ray plate because of the natural anterior curve in that region. It has not the same shape that the other lumbar vertebrae have, being wedge-shaped, with the narrow edge of the wedge directed backward. It is also bound to lie at an angle with the roentgen-ray plate, because its axis is directed backward and upward. The roentgen rays, therefore, fall obliquely upon it and through it, and the shadow cast on the plate is necessarily ill-defined. The lumbosacral region of the spine is a meeting place of wedges of the sacrum and body of the fifth lumbar vertebrae, and is always far removed from the roentgen-ray plate. It has, therefore, two anatomic disadvantages which are evident when one endeavors to obtain a correct shadow, and interpretation of the roentgenogram must be made with care.

It is indeed essential to remember the foregoing facts, and to try to reduce the lordosis of the lower part of the spine to a minimum, by asking the patient to flex the hips slightly when the roentgenogram is taken, in that way bringing the lower part of the spine nearer to the plate.

---

3. McKendrick: Footnote 2, p. 6.

In my own practice, I have lately adopted the method suggested by McKendrick, taking a roentgenogram of the lower part of the spine at first with the body fully extended, following it by another exposure with the lower extremities slightly flexed, so as to reduce the lordosis to a minimum. From the two findings, one can ascertain the mobility of the spine in that region, by comparing the distance between the spinous processes of the lower lumbar vertebrae in the two plates.

MECHANICS OF THE SPINAL COLUMN

To quote from Keith:[4]

> When we look at the naked back of a man sitting or standing in front of us, we are really looking at one of the most wonderful acrobatic feats to be seen in the animal kingdom. In such an attitude, twenty-four segments, or vertebrae, are being delicately and steadily balanced, one upon the other, by means of the elaborate system of levers, and muscles with which each vertebra is furnished. The intervertebral disks on which each vertebra is poised are at once one of nature's oldest and most ingenious contrivances. It is a water-cushion surrounded by a strong, but loose ligamentous covering. Only when the spine is bent or rotated do these ligaments, which enclose the intervertebral cushion, become stretched, the fibers on the convex side of the curve become taut and strained, while those on the concave side of the curve are flexed and bent outward. The lowest vertebra of this flexible, weight-supporting spinal rod is based on the sacral or pelvic cushion; on the highest is poised the head.
>
> The leverage and motor system of an individual vertebral segment, is best seen in a vertebra taken from the dorsal region. The posterior or spinous lever bifurcates at its root so as to enclose and protect the spinal cord; an elaborate system of muscles is attached to the spinous lever, whereby the vertebral body may be maintained in its correct antero-posterior plane. On each side of the vertebra is placed a lateral lever, rendered enormously powerful by being prolonged as a rib. These lateral levers are also furnished with elaborate sets of balancing muscles. In the living upright spine, every one of these muscles—about eight to each vertebral segment, making about two hundred in all—is called into action, not by any conscious effort of the will, but by that reflex mechanism which automatically governs all the static actions of the human body.

Hence, we see that the human spine is a mechanical contrivance skilfully arranged to keep us in upright posture, and has the greatest strength compatible with lightness and flexibility.

So far we have spoken of the mechanical advantages of the spinal column. However, in order to understand pathologic conditions involving the spine, it is also necessary to enumerate its mechanical disadvantages.

(*a*) The spine as a column: If we observe the shape of the spinal column when viewed anteriorly, we see that it has different dimensions in different parts, and that the base of the pedestal, where its rests on

4. Keith: Menders of the Maimed, pp. 171-172.

the sacrum is the broadest part. It gradually becomes narrower until it reaches a little above the middorsal region. From here, it again broadens out gradually until the seventh cervical is reached, when it again becomes narrower, up to the first cervical vertebra.

(*b*) Differences of mobility in the various portions of the spinal column: Owing to certain factors, which will be pointed out in the latter part of the article, the spinal column is made up of some parts which are freely movable and others which are restricted in motion, some portion with almost no motion at all, some with very little if any anteroposterior motion, while others again have only provision for lateral deviation and rotation.

(*c*) Junction of the various curves, which are easily demonstrable when the spine is viewed from the lateral aspect: These factors enumerated above, constrictions exhibited in the spinal column, the junction of various curves, various movements and the junction of flexible with less flexible segments constitute mechanical weaknesses, and the sites involved are at a great mechanical disadvantage when the physiologic limits of function are exceeded.

To illustrate: McKendrick quotes Menard with reference to the frequency of fractures in the various parts of the spine. Of 384 cases reported, the sites of the injury were divided as follows: seventh cervical, 12; second dorsal, 10; third dorsal, 8; fourth dorsal, 9; fifth dorsal, 15; sixth dorsal, 10; seventh dorsal, 10; eighth dorsal, 20; ninth dorsal, 25; tenth dorsal, 32; eleventh dorsal, 37; twelfth dorsal, 80; first lumbar, 78; second lumbar, 23; third lumbar, 6; fourth lumbar, 7; fifth lumbar, 1.

From the foregoing, it is evident that the greatest number of fractures of the spine take place between the eighth dorsal and the second lumbar, and the number of injuries increase as we descend the spinal column in the dorsal region, where it reaches its climax at the last dorsal; while on the other hand, in the lumbar region, the reverse condition holds true, the highest number being at the first lumbar and the number decreasing as we go down the column to the last lumbar.

In conjunction with the foregoing statistics, it is worth while remarking that in tuberculosis of the spine the same rule holds good. Thus, Whitman gives statistics of 475 cases of Pott's disease treated at the Hospital for Ruptured and Crippled, of which 321 cases presented involvements of the dorsal region, and 154 cases lumbar affections, divided as follows: first dorsal, 6; second dorsal, 7; third dorsal, 12; fourth dorsal, 10; fifth dorsal, 19; sixth dorsal, 17; seventh dorsal, 33; eighth dorsal, 36; ninth dorsal, 36; tenth dorsal, 43; eleventh dorsal, 38; twelfth dorsal, 64; first lumbar, 59; second lumbar, 37; third lumbar, 31; fourth lumbar, 17; fifth lumbar, 10.

Lovett, in his statistics, taken from the Children's Hospital of Boston, of 1,792 cases of spinal tuberculosis treated during the years 1883-1907, finds the locations affected as follows: cervical or cervicodorsal, 247; dorsal or dorsolumbar, 1,025; lumbar, 329; insufficient data, 191; total 1,792. Of a series of 209 cases of back affections treated at the University and Bellevue clinic in the last few months, thirty-five were tuberculous, the lesions being distributed as follows: four in the cervical region; nineteen in the dorsal, and eleven in the lumbar.

Muscles Acting on the Back.—It is interesting to note that, when speaking of muscles acting directly on the back, we are dealing with very few powerful muscles which act thus by vocation. All the other muscles with extensive origin in the spinal locality act on the spine by avocation only; for, owing to the fact that their insertion is elsewhere, it is there that we must look for their real function. Thus, flexion of the spine is produced directly by contraction of pairs of muscles that are situated in front of the spine: rectus abdominis, external and internal oblique, assisted by sternohyoid, sternothyroid, sternocleidomastoid, thyrohyoid, mylohyoid, digastric, scalenus anterior, longus colli and longus capitis; while, in the lower part of the body, the direct flexors are assisted by the psoas magnus and parvus and quadratus lumborum.

The extensor muscles are those muscles which extend the spine by the equal and combined action of pairs of muscles, situated on either side of the spinal column, and in a plane posterior to the axis of movement of the spine. If the muscles on one side contract more powerfully than those on the other side, lateral bending of the body or bending with rotation is produced. Following is the list of extensors when acting equally in pairs: erector spinae, semispinalis, multifidus spinae, rotatores spinae, interspinales, serrati posteriores, splenus and, when the scapula is fixed, levator anguli scapulae and the upper fibers of the trapezius.

When the origin and direction of the various muscles enumerated above are studied, it is found that the only muscles which are in reality powerful and direct extensors of the spine are those situated in the lower part of the spine, the fleshy part of the erector spinae, assisted mainly by the multifidus spinae; for higher up in the dorsal region of the spine, the offshoots of the erector spinae and the multifidus are unique by their abundance and delicate arrangement, as well as the direction of the fibers, with consequent variegated and multitudinous function. From the direction of these fibers, it can be seen that they were meant for rotation and lateral motion rather than extension.

"It is interesting to note," MacKenzie remarks, "that there is no prevertebral muscle in the thoracic region of the spine, where flexion

and extension are practically absent. Extending force in that region must be exerted chiefly against gravity." [5]

In view of the fact that there is a constant struggle of the body to maintain its erect posture, the muscles of the back as well as all the muscles which have to maintain the upright and standing position of the body are always under tension, as Arthur Keith so aptly puts it "clutched"; and it is probably the weakness of the nerve response and the lowering of the tonicity of the strong muscle fibers which contributes to the usual tendency of the aged person to stoop forward. For "there is no such state as skeletal balance apart from the muscular action." [6]

The paucity of powerful extensors per se in the dorsal region may account for the marked kyphosis that usually takes place in tuberculous involvement of that portion of the spine. The muscles of the dorsal vertebrae, being mostly concerned with rotation, are not properly prepared to cope with the situation, and, as a result of the breaking down of the bodies of the vertebrae, an approximation of the vertebral bodies and flexion of the spine takes place, while in the lumbar and cervical regions, the extensor muscles, being abundant, are prepared to meet the emergency by exaggerating the lordosis through contractions.

Rôle of the Musculature of the Spine in the Production and Maintenance of the Deformities of the Spinal Column.—Painstaking investigation convinces me that, in the muscular system of the spine, we can find the main solution to the problem of many deformities of the spine. Perhaps some of the results achieved in various operative procedures which have mistakenly been ascribed to other causes may have resulted from the fact that some of the muscles that have hindered the spine in readjusting itself have been put out of commission or rendered innocuous by such operation, and in that way, the rotation of the spine, which is always produced by the muscles, has been checked by adequate subsequent support.

It is interesting to observe the reaction of the muscles of the spine to electrical stimulation in the early and later cases of curvature. In early cases, there seems to be hypersensitiveness of the convex part of the dorsal curve to electrical stimuli. A mild current which ordinarily would not excite a reaction in a normal person may produce pain if applied in such early cases, and the spinous processes of the stimulated region will rotate to the other side away from the contracted muscles. In stimulation of the muscles on the side on which the concavity of the curve is situated, a much greater stimulus is needed to get a reaction, some times as much as three times the strength of the stimulus

5. MacKenzie: Action of Muscles, London, H. K. Lewis & Co., 1919, p. 217.
6. MacKenzie: Footnote 5; p. 219.

needed to get the reaction on the convex side. Then, when a reaction does take place, it does not have enough power to turn the spinous processes over to the other side, but stimulates the muscles of the concave side so that the spine will straighten somewhat by pulling the column toward the center.

If the stimulus is applied in the lumbar region, imperceptible rotation of the spinous processes takes place, toward the side opposite to the stimulus; but the movement most marked is the anterior extension or hyperextension of the lumbar spine and exaggeration of the lordosis, as well as a lateral movement of the body, with the concavity toward the stimulated side. In the more advanced cases of rotary curvature, the stimulus, when applied to the convex side, will eventually produce some reaction, provided the stimulus is excessive, but no movement or rotation of the spine takes place. The concave side gives no reaction at all, or a reaction of degeneration.

Electrical stimulation applied to the normal spine gives the following characteristic reactions: When both applicators are applied to one side of the dorsal region, the upper six or seven dorsal vertebrae, while the person is in prone position on the table, and the arms are so held that the posterior muscles of the shoulder are somewhat contracted and the scapulae approximate each other, there is a marked contraction of the muscles in that region to a medium stimulation, with the rotation of the spinous processes of the stimulated side to the opposite side, resulting in a slight lateral bending so as to form a curve with the convexity away from the side stimulated. If the stimulation is marked, the muscles of the entire length of the spine seem to respond, even though the electrical stimulation is applied to the upper dorsal region only.

While there is a rotation and lateral bending of the upper dorsal as previously mentioned, only the lumbar region cooperates in the activity through the contraction of its muscles, bending laterally to the side of the contraction, which is the same side as the curve formed at the dorsal region. The middorsal does not seem to be affected to the same degree. On the other hand, if the arms are slightly abducted and placed in a position so as to relax the trapezius and get the scapula away from the spinous region, a stimulus applied to the region of the locality mentioned above (the upper six or seven dorsal) will produce a rotation of the spinous processes over to the side of the stimulation, and produce a slight convexity in that region; while the concavity will be directed to the opposite side.

If the stimulus is stronger, the lumbar muscles will also contract on the same side, but the rotation of the spinous processes in the lumbar region will be as before, toward the relaxed side, forming a concavity toward the contracted side, with the convexity away from

the stimulated side. If an electrical stimulus is applied to the lumbar region exclusively; if on one side only there is a lateral bending with the concavity toward the stimulated muscles and a slight increase of the lordosis in that region, such contraction will have little influence on the motion of the upper dorsal, unless the applicators are so applied that one of them is on the lower part of the lumbar region, and the other a little away from the spinous process at the tenth or eleventh dorsal.

I am speaking of these reactions in order to make clear the fact that, in the spine, we are dealing with antagonistic groups of muscles finding their origin and insertion on the same side of the back; and as in antagonistic groups of muscles found elsewhere, there must be an accompanying inhibiting stimulus to one group while the other group is to act. We can therefore understand that it is possible for a deformity to occur in the spine due to manifold causes: (1) the group that was supposed to hold the other in check became weak, and hence was unable to do its inhibitory work sufficiently and in that way left the field entirely to the other group; (2) the inhibitory muscles may have become overstimulated, and contracted, either permanently or temporarily, owing to some irritation, and in that way interfered with the function of the normally working muscles of the same side, or (3) infantile paralysis or rickets, or other diseases, while interfering with the proper nerve conductivity of one side of the back, have given a chance to the muscles of the opposite side to work unhampered, and in that way embarrassed the working of the spinal column and the maintenance of its proper equilibrium; for "there is no such state as skeletal balance apart from muscular action."

Another possibility to be thought of is that, owing to some systemic condition or infection, there may be an interference with the nerve conductivity of both sides of the back of either both groups of muscles or one, and in that way the function of the column can be interfered with.

Now, with the exception of malformation of the spinal column of one vertebra or a group of vertebrae, which we may term congenital, provided we are sure of our ground, we can very well understand how it is possible for vertebrae to become misshapen and deformed as a result of muscular stress, if the latter either singly or in a group is permitted to have full play over any vertebra in its entirety or in part. We must not forget the fact that bone formation and shape is largely determined by pressure stresses and functional pressure, and the earlier such bone is exposed to these pressure functions and pressure stresses, the greater will necessarily be the influence on the form and shape of that bone. In the vertebral column, we are dealing with about forty-six growth cartilages of the bodies proper; many more for the

spinous and transverse processes, and about 200 muscles acting on the bone. We can therefore easily understand the great influence that the musculature of the spine is bound to exert on the form and shape as well as on the growth of the vertebrae and its various portions.

Now the fact that children are more exposed to various infective influences and that there is a constant struggle against these influences by the formation of various immune substances in the blood is something that even a tyro in medicine is aware of. The various infectious diseases so prevalent in childhood bear mute testimony to this fact. The child is also exposed to dietary indiscretions, which will exert a great influence on its growth. Exercise of a certain group of muscles, when too frequent, will stimulate that group to greater activity, with consequent deleterious effect on the opposite group, and with an added stimulus to the growth cartilage affected by the pressure and functional stresses imposed on it, which may eventually lead to a weakness of the over-exercised muscle group itself, for reasons to be given later.

Why do injurious agents first affect the muscles and then the skeleton?

Dr. Murk Jansen, in his book dealing with "Feebleness of Growth and Congenital Dwarfism," answers that question in an ingenious way.

> The muscles constitute 25 per cent. of the body weight in the new-born child, 43 per cent. in the adult. No tissue in the body, therefore, demands so much of the power of growth, and it is only rational that a lack of the power of growth should make itself felt wherever the exigencies of growth are greatest. The law of vulnerability of fast growing cells, according to which the vulnerability of cells is proportional to the rapidity of their growth, therefore, throws light on the fact that feebleness of growth first manifests itself in the muscles. After the musculature, the skeleton demands the most growth; for it forms 13.5 per cent. of the body weight in the new-born child, and rises to 17.5 per cent. in the adult. In harmony with the foregoing law, that the faster the growing cells, the greater their vulnerability, is the fact that, in the skeleton, the growth cartilages are the first to be affected; while in the more severe cases, the diaphysis follows, and in the choice of the growth cartilage the organism shows its conformity to this law. It is generally known that in the second year of life, the time when the child begins to walk, the legs lengthen more rapidly in proportion to the trunk. This continues up to adult age, and during these years the four growth cartilages of femur and tibia add more to the height of the body than do the forty-eight growth cartilages of the vertebrae. It is equally well known that the lengthening of the lower extremities is for the greater part achieved by the growth cartilages near the knee. The rapidity of their growth therefore exceeds that of the vertebral growth cartilages over twelve times. In harmony with this, the fact presents itself that children with moderate feebleness of growth have a tendency to develop knock knees, especially after they begin to walk. Before that time is the period when the growth of the trunk predominates, i. e., the time of the development of deformities of the ribs and the

spine. From these considerations, it is pretty safe to lay down the rule that in the scoliotic or humpback with straight legs (without either knockknees or bowlegs) the development of their lateral curvature dates back to the time before they had started to walk.[7]

THE COMMUNICATING MECHANISM BETWEEN THE SYMPATHETIC AND THE CEREBROSPINAL NERVOUS SYSTEM AND ITS RELATIONSHIP TO THE MOBILITY OF THE SPINE

It is important to observe that the cerebrospinal nervous system is intimately connected and in close relationship with the sympathetic system through the white and gray communicating fibers. The white communicating fibers come from the spinal nerves and run to the sympathetic chain, while the gray fibers run from the sympathetic chain to the spinal nerves at their exit. Though in the cervical vertebrae the sympathetic ganglions are abundant, none of their fibers seem to be attached to either the vertebrae or the ligaments. On the other hand, there are sympathetic fibers supplying the vertebral bodies directly as well as their ligaments in the upper six dorsal and in the lumbar region; but there are none in the lower dorsal. If one bears in mind that the sympathetic branches in the dorsal region also supply filaments to the thoracic aorta and its branches, and that in the lumbar region the internal branches which supply filaments of sympathetic fibers to the vertebrae of that region also help to form the aortic plexus, and in conjunction with other branches play an important rôle in the formation of the hypogastric plexus, the direct effect of changes in the various parts so intimately connected, be they slight or severe, functional or organic, becomes at once apparent.

The importance and significance of the vast intercommunication of the sympathetic with the cerebrospinal nervous system is well brought out by Langdon Brown.

> This fact that internal sensations have a cutaneous representation has provided us with a valuable method of localizing visceral disorders, as had previously been pointed out by Ross and James MacKenzie. A pin is drawn lightly over the surface of the body, and at a certain point its contact becomes distinctly painful. By repeating the process in different directions, a zone is mapped out. Knowledge of the corresponding viscera, innervated by the same spinal segment, enables us to locate the sources of the internal pains.
>
> In many diseases of the stomach, particularly ulcer, there is a zone corresponding to the tenth left dorsal segment, which includes the umbilicus. In duodenal ulcer, the tenth right thoracic segment may be found hyperesthetic; in angina pectoris, the axillary portion of the third and fourth left thoracic; in gallstone, the ninth right thoracic. Such zone may not correspond with the local tenderness elicited by pressure which depends upon deep sensibility in the

7. Jansen, Murk: Feebleness of Growth and Congenital Dwarfism, Oxford Medical Publications, 1921, pp. 19-20.

inflamed structure. Thus, in gastric ulcer the epigastric tenderness is distinctly higher than the zone of hyperesthesia. This tenderness, as Hurst showed, is located by the brain according to the average position of the part in which it originates, and the localization is accordingly most accurate in those viscera which are most fixed.[8]

Dr. James Madison Taylor,[9] in studying fifty cadavers, in order to determine the relationship between malformations of the body segments and visceral disease, finds that "many visceral affections were found associated with minor curves of vertebral segments belonging to the same sympathetic segments as the affected organs."

Hence, we can very well understand how, owing to the abundance of the sympathetic nerve supply to the pelvic and lumbar regions, and the intimate connection of that nerve system with the bodies of the vertebrae as well as the ligaments and muscles of that region, because of its direct supply as well as that through the communicantes, any disturbance of the internal organs will directly affect the lumbar spine and also its musculature, producing a contracture of these muscles, and in that way interfering with free mobility of that region. On the other hand, the free movements of the lumbar spine, stretching the ligaments and muscles, will have a tendency to stimulate the internal abdominal and pelvic organs to greater activity through its effect on the sympathetic nervous system.

MOBILITY OF THE SPINE

McKendrick emphasizes the absence of flexion of the spinal column in the dorsal region, and insists that there is an absence of lateral flexion and a limitation of rotation in that region. He substantiates his statements by photographs and measurements of the spine, and the distance between the various segments, with the subject in various attitudes.

In measuring the back, with the subject standing erect, the distance was as follows: first dorsal, 0 inch; twelfth dorsal, 12 inches (30 cm.); fourth lumbar, 16½ inches (41.25 cm.); posterior-superior spine of ilium, 18¾ inches (46.8 cm.).

With back fully bent; first dorsal, 0 inch; twelfth dorsal, 12 inches (30 cm.); fourth lumbar, 18 inches (45 cm.); posterior-superior spine, 21 inches (52.5 cm.).

In other words there is a distance of 4½ inches (11.25 cm.) between the last dorsal vertebra and the fourth lumbar when in the erect posture, and this increases by 1½ inches (3.7 cm.) during full flexion. There is a distance of 1¾ inches (4.3 cm.) between the fourth lumbar

8. Brown, Langdon: The Sympathetic Nervous System in Disease, Oxford Press, 1920, pp. 17-18.

9. Taylor, J. M., and Winsor: Preliminary researches.

and the posterior-superior spine in the erect posture and this increases by 2¼ inches (5.6 cm.) in extreme flexion. With these measurements, McKendrick [10] proves how much greater the range of movement is between the lower lumbar vertebrae than between the upper. He also points out an important fact that to this free motion of the lumbar is due the fact that in many cases in which fractures occur in the upper lumbar region, the patient recovers without any restriction in the movement of the spine.

My own investigations bear out the conclusions of McKendrick so far as his findings of the free mobility of the lumbar region is concerned (anteroposteriorly); also as to his observations with reference to the greater mobility between the joints of the lower lumbar vertebrae than between those of the upper. I cannot subscribe to his statement as to the immobility of the dorsal. As stated before, an electrical stimulus to the upper part of the dorsal, provided it is moderately vigorous, will elicit a marked response by rotating the upper six dorsal spinous processes to the other side with lateral deviation, so as to form a convexity to the other side of the stimulated region. The lower dorsal does not seem to accompany the reaction to the same extent, this proving that the motion in the upper dorsal is partly segmental, and not a simple rotation of the entire dorsal column on the cervical above and the lumbar below. Roentgenograms of the dorsal and lumbar spine with the patient in flexed position, the exposure being made laterally, show that there is no anteroposterior motion in the middorsal; and none occurs until we reach the ninth dorsal. From the ninth dorsal downward, one can see an approximation of the anterior parts of the bodies of the vertebrae, and a corresponding widening of the intervertebral spaces posteriorly (the patient being in the same flexed position); coming nearer in their function to the lumbar vertebrae, where the anteroposterior motion and the effect on the intervertebral spaces is more easily discernible.

Measurements taken of the distances of the various parts of the spine in various positions, with the accompanying photographs, showed that (1) there is some anteroposterior mobility in the last three or four dorsal joints, and (2) the entire dorsal column is very poor in its mobility anteroposteriorly, as well as in its lateral motion. Photographs were taken with the subject standing erect, then bending forward, and then bending laterally, the distance between the various parts of the spinal column measured as each pose was assumed by the subject being given in Table 1.

A comparison of measurements (in inches) with the same subject in an erect posture and bending laterally is given in Table 2.

---

10. McKendrick: Spinal Injuries, p. 20.

Now, what do these measurements show? First, that whereas in forward bending the distance between the seventh dorsal and the last dorsal is increased by 1 cm. only, the distance between the latter and the last lumbar (inclusive) is increased from 12.75 to 17.5 cm. There is a still greater separation, comparatively, between the fourth and the fifth lumbar in forward bending, than there is between the last dorsal and the fourth lumbar; for, whereas the distance between the last dorsal and the fourth lumbar was 9.75 cm., and increased to 12.5 cm.

TABLE 1.—*Spinal Column Measurements*

	In Erect Posture Cm.	Bending Forward Cm.
1. 1st dorsal	0	0
2. 7th dorsal	17	18.5
3. From 7th to 12th dorsal	14	15
4. From 12th dorsal to lower part of 4th lumbar	9.75	12.5
5. From 4th to posterior-superior spine (5th lumbar)	3	5
6. From 5th lumbar to most prominent part of the sacro-iliac synchondrosis	4	6

TABLE 2.—*Comparison of Measurements*

	Erect Posture Inches	Bending Laterally Inches
1.	0	0
2.	7	7¼
3.	7	7
4.	3½	4
5.	2	2½

in forward bending, the distance between the fourth and fifth lumbar, being normally in my subject 3 cm. when erect, increased to 5 cm. in forward bending. Another important point in connection with the foregoing measurements is the fact that there seems to be quite a little mobility in the lumbosacral joint; for while the distance between the posterior-superior spinal line and the most prominent portion of the sacro-iliac synchondrosis equaled 4 cm. in my subject when standing erect, there was an increase of 2 cm. when the subject was bending forward. The lateral motion in that region will naturally be determined by the proximity of the transverse processes to the crest of the ilium, which seems to vary in almost all persons (Figs. 1-5).

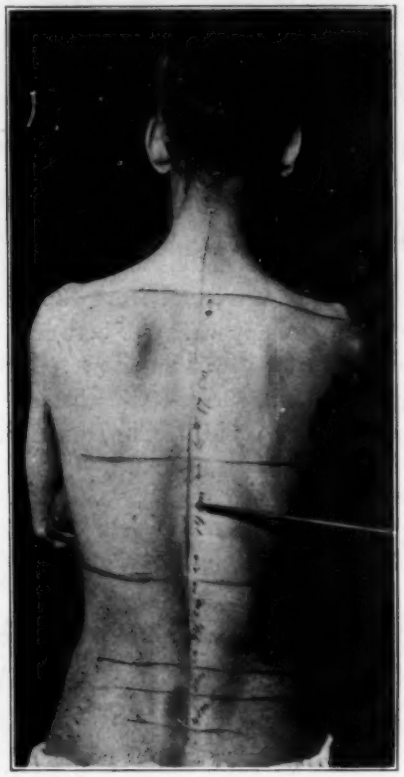

Fig. 1.—Measurements with subject in erect position.

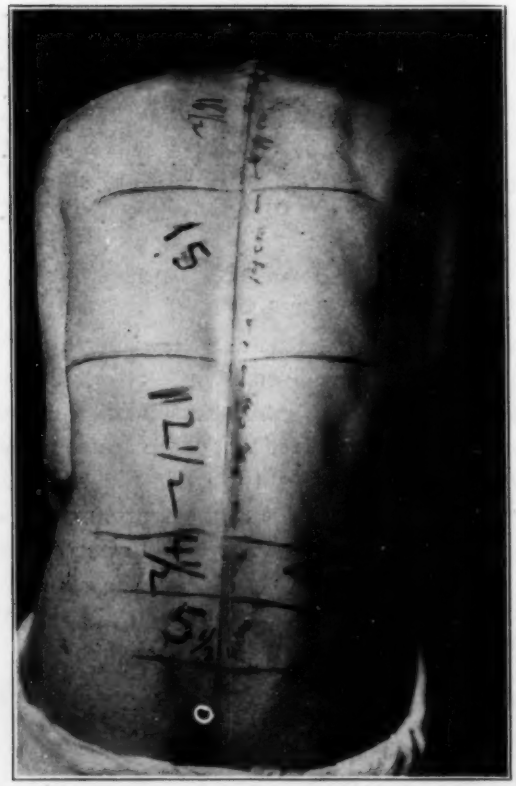

Fig. 2.—Same subject as in Figure 1, bending forward. The numbers on the left show the increase in the interlinear spaces.

PRACTICAL IMPORTANCE OF FOREGOING OBSERVATIONS

In view of the fact that the lower part of the dorsal has mobility, it, as well as the lumbar, is subject to strain. This observation is at variance with the conclusions of McKendrick Lovett,[11] in speaking of tuberculosis of the spine, remarks that the lower dorsal region is affected much more often than the upper. Thus, of 321 cases of spinal tuberculosis, only seventeen were in the upper six dorsal vertebrae, and 250 in the lower six. And he attributes it to the fact that the disease apparently locates itself in the region of greatest mobility (the dorsolumbar), suggesting the influence of trauma in its localization.

Lovett's remarks do not coincide with the proven facts; for the foregoing measurements substantiated by roentgenograms and photo-

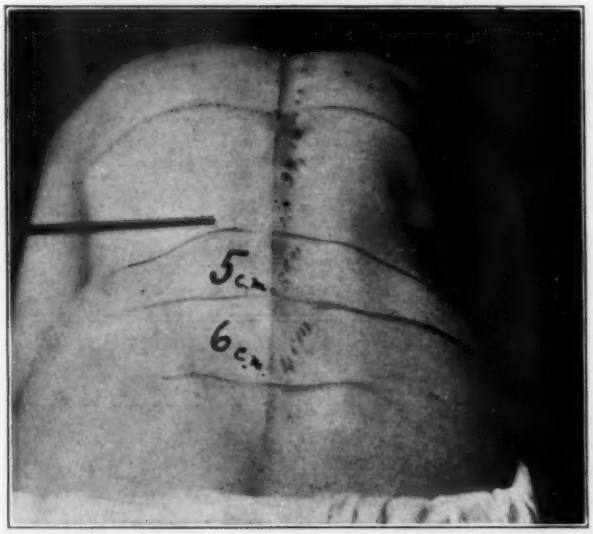

Fig. 3.—Subject in extreme forward flexion. The widening of the lower two interlinear spaces may be noted.

graphs show conclusively that there is a greater mobility in the lower part of the lumbar than in the upper, and yet the smallest number of tuberculosis cases occur in the lower part of the lumbar spine, especially between the fourth and the fifth lumbar.

It seems therefore more reasonable to assume that the greater frequency of the disease in the dorsolumbar region is rather due to the mechanical disadvantages of the spinal column in that region, as previously mentioned. Since the lower dorsal vertebrae are situated

11. Jones, Robert, and Lovett, R. W.: Orthopedic Surgery, New York, William Wood & Company, 1923, p. 201.

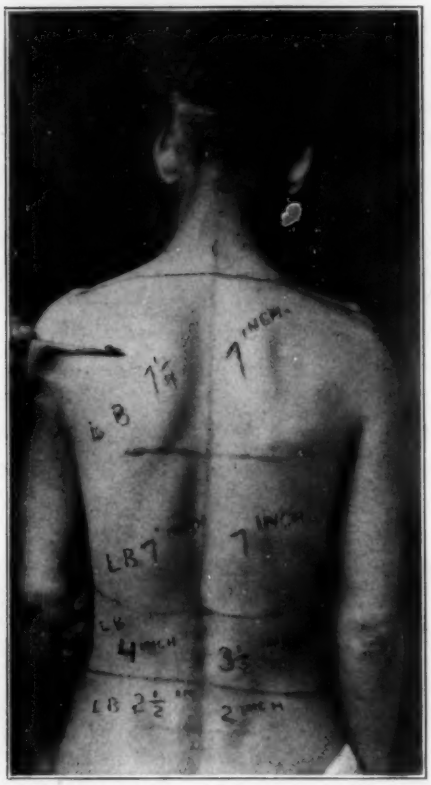

Fig. 4.—Measurements with subject in erect posture. Numericals to right represent these measurements.

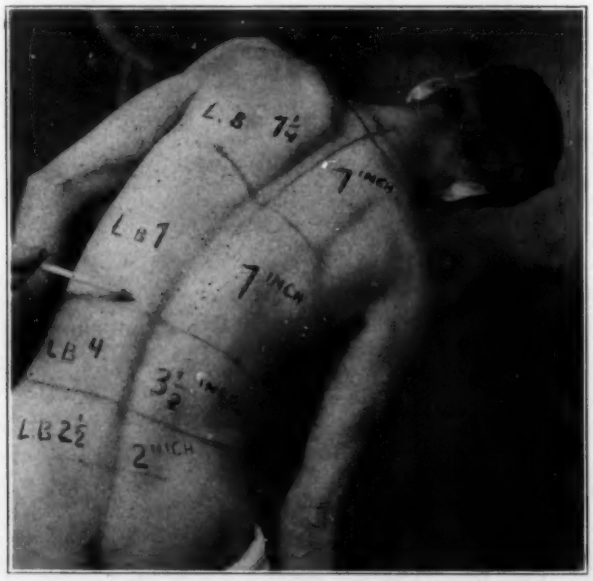

Fig. 5.—Measurements with subject bending laterally. Numericals to left represent these measurements.

between a freely movable column below and a nonmovable column above, they suffer more frequently. Were free mobility of a joint the sole cause for the frequency of tuberculous involvement, the shoulder joint, having the greatest mobility, should be the joint most frequently attacked. But all observers agree that the shoulder joint is the joint least often attacked by tuberculosis. Lovett himself, in speaking of tuberculosis of the shoulder, says: "The disease is uncommon in this location in childhood, and, in both children and adults, tuberculosis of the upper extremities is much less common than that of the lower. At the Boston Children's Hospital, in 7,474 cases of tuberculosis of the spine and joints, only seventeen involvements of the shoulder joints were noted." [12]

That the lower dorsal bears the brunt of stress and pressure is shown by the fact that, in marked rotary curvature of the spine of long standing, one will find that the vertebrae of that region are the ones most affected in shape and size, showing that the rotation takes place around this region; and it is therefore this locality that is caught between the freely movable and an entirely unmovable portion of the spine.

Before proceeding with the consideration of the clinical application of the previously discussed observations, it is important to study one of the most frequent deformities of the spine with which the human species is afflicted, lateral curvature.

It seems to be the opinion of those who have not made a serious study of the subject that the disease commonly afflicts women. Statistics carefully collected prove that this contention is wrong. Though it is true that the majority of curvature cases treated in any orthopedic clinic are female, the number of male patients suffering from the deformity is by no means small. Thus, at the University and Bellevue Orthopedic Clinic, we have treated, during 1922, 216 cases of spinal disease, sixty-three of which were cases of lateral curvature, divided as to sex thus: male, twenty-three; female, forty. Lovett, in speaking of the sex incidence in scoliosis, makes the following interesting observation:

> It is generally the opinion that in adults women show a greater number of scolioses than men, although published statistics confirming these facts do not exist. Records of the relative frequency of scoliosis in adolescents and children made in orthopedic institutions where patients apply for treatment show a very much larger percentage of scoliosis among girls than in boys. The difference between the sexes is less where large numbers of school children are investigated, such figures showing in general a slightly higher percentage in girls than in boys. To explain this difference, we must either assume that boys out-

12. Jones and Lovett: Footnote 11; p. 186.

grow scoliosis, or that they do not come to the institutions for treatment until the curves become severe, or until complications arise, while in girls the effects of scoliosis upon the figure are perceptible much earlier, and treatment is sought to remedy curves which in boys would pass unnoticed by the parents.[13]

The figures bearing on the sex of scoliotics treated in our own institution differ greatly from statistics culled from other observers. Lovett presents the figures quoted in Table 3, on sex incidence in scoliosis as observed by various authors.

TABLE 3.—*Sex Incidence in Scoliosis*

Authors	In Boys Per Cent.	In Girls Per Cent.
Eulenberg	13	87
Ever	7	93
Ketch	17	83
Kolliker	20	80
Roth	8.5	91.5
Wedberg	15.9	84.1
Behrend	13.4	86.6
Adams	12.8	87
Scholder	14.8	85
Schantz	25	74.8
Rosenthal	22	78
Schulthes	14.2	85.5
Redard	15.6	83.3

The reason for the discrepancy between our statistics and the statistics of others is the fact that many male patients in our clinic are adults who come to the clinic because of pains in the spine, and incapacity to do a full day's work; while the female patients who are being treated for curvature of the spine at our clinic are young girls; this rather bearing out the contention of Lovett quoted before.

Whatever other reasons for the preponderance of curvature in females may be, one thing is certain: there is one part of the spine which differs in shape, angle of projection and size in the two sexes, especially so at puberty, and that is, the lumbosacral region.

Gray, in speaking of the differences in the sacrum of the male and the female, says:

The sacrum in the female is usually wider than in the male; the lower half forms a greater angle with the upper, the upper half of the bone being nearly straight, the lower half presenting the greatest amount of curvature. The bone is also directed more obliquely backward, which increases the size of the pelvic

13. Lovett, R. W.: Lateral Curvature of the Spine, Ed. 3, Philadelphia, P. Blakiston's Son & Co., p. 113.

cavity; but the sacro-vertebral angle projects less. In the male, the curvature is more evenly distributed over the whole length of the bone, and is altogether greater than in the female, and the sacro-vertebral angle projects more forward.

Again, in speaking of the pelvis, Gray emphasizes the differences between the female and the male pelvis:

The female pelvis, looked at as a whole, is distinguished from the male by the bones being more delicate, by its width being greater and its depth smaller. The whole pelvis is less massive, and its bones are lighter and more slender, and its muscular impressions are slightly marked. The iliac fossae are broad and expanded, and the anterior iliac spines widely separated; hence the greater prominence of the hips. The inlet in the female is larger than in the male. It is more nearly circular; and the sacro-vertebral angle projects less forward. The cavity is shallower and wider; the sacrum is shorter and wider and its lower half forms a greater angle with its upper.

In the foetus, and for several years after birth, the pelvis is small in proportion to that of the adult. The cavity is deep, and the projection of the sacro-vertebral angle less marked. The antero-posterior and transverse diameters are nearly equal. About puberty the pelvis in both sexes presents general characters of the adult male pelvis; but after puberty it acquires its proper sexual characters.[1]

The sacrolumbar region of the spine is therefore the part which undergoes changes in size, shape and angular deviation at a time when the rest of the spine is growing very slowly. The intervertebral cartilages of the upper segments of the sacrum begin to disappear and ossify, at about the twentieth year, and any irritation in this locality will certainly have great bearing on the form and shape of the beforementioned region. Again, the powerful muscles located in that region, which are necessary in order to maintain the erect posture of the body, will have a tendency to further the production of deformity in this region in case the median pull of these muscles is interfered with.

Anyone who has examined a large number of roentgenograms of the spine will be struck by the small number of normal fifth lumbar vertebrae. So small indeed is the number that one can almost say that the exception has been taken for the rule. McKendrick [14] claims to have examined 20,000 plates of the spinal column, paying particular attention to those of the lumbosacral region. The majority of those plates were taken, not to determine the condition of the spine, but for purposes of diagnosis in genito-urinary cases; so that the question of trauma could be excluded. McKendrick found many articular processes varying greatly and often presenting an appearance which suggested diagonal crushing of the vertebra in question. Even a diagnosis of dislocation would sometimes have been excusable, the laminae being off the horizontal plane, giving the vertebra an appearance of having been tilted.

14. McKendrick: Footnote 10, p. 121.

In quite a number of cases, a developmental malformation was apparent, and he concludes with the pertinent remark that it is little wonder that damage is often diagnosed in this locality (lumbosacral) when none exists. He further advises that, in order to avoid slipping into this error, the following points be considered: 1. Could the violence possible have produced a fracture in this particular region? 2. Do the symptoms and signs point to gross damage to the base of the spinal pedestal? 3. Is the diagnosis of damage here justifiable from roentgen-ray examination alone?

McKendrick is right in his contention that one must be on his guard against diagnosing every apparent deviation from the normal in the lumbosacral region as due to trauma, unless it is accompanied by additional changes in the environment, be they bony or muscular, causing a change in the normal appearance of the part; provided also that additional symptoms and signs are present to warrant a diagnosis of injury or disease in that locality. On the other hand, many congenital malformations may very well remain unnoticed for a long time, until a systemic disease or a slight injury will select that particular locality because of its weak resistance, due to the malformation. To illustrate: Slight fatigue of back muscles will produce round shoulders when there is failure of fusion of the lamellae in the last lumbar vertebrae, which results in a weak union of the lumbosacral articulation. (I had one similar case.) Failure of fusion of the sacral vertebrae in an adult will expose that person to a strain of the lower part of the spine at the slightest provocation. (There were two such cases in our clinic.)

In the many hundreds of spinal cases that I have examined in the various clinics, as well as in my private practice, I have made it a rule to examine the patient first, taking notice of and jotting down the slightest deviation from normal, which can be ascertained by observation, palpation, percussion, etc. A tentative diagnosis is then made and a roentgen-ray examination ordered for corroboration and assistance. In going over the cases of spinal curvatures in this way, constantly checking up my clinical findings with the roentgenograms, I have been impressed with the following facts:

1. In the majority of cases of curvatures of idiopathic origin, one will find a pathologic alteration in the sacrolumbar region, and hence, even in perceptible dorsal curves, unless the examination, physical as well as roentgenographic, includes also the lower lumbar region, it is valueless. There seems to be in all these cases a deviation of either the sacrum carrying along the last lumbar, or a deviation of the last lumbar per se, with a thickening or hypertrophy of one side of the lower part of this vertebra at its junction with the sacrum, throwing the body of the vertebra over to the other side, and threatening in that way the equilibrium of the spinal column (Figs. 6 and 7).

2. In view of the fact that the concavity of the lumbar curve, even in very early cases, is always formed in the direction of the hypertrophic part of the last lumbar, contrary to gravity, it seems to me to be a resistant curve, designed to counteract the wrong pull of the last lumbar, rather than a primary curve, and the position of its concavity is further assisted by the contractures of the quadratus lumborum and multifides spinae muscles on the concave side, and probably the psoas.

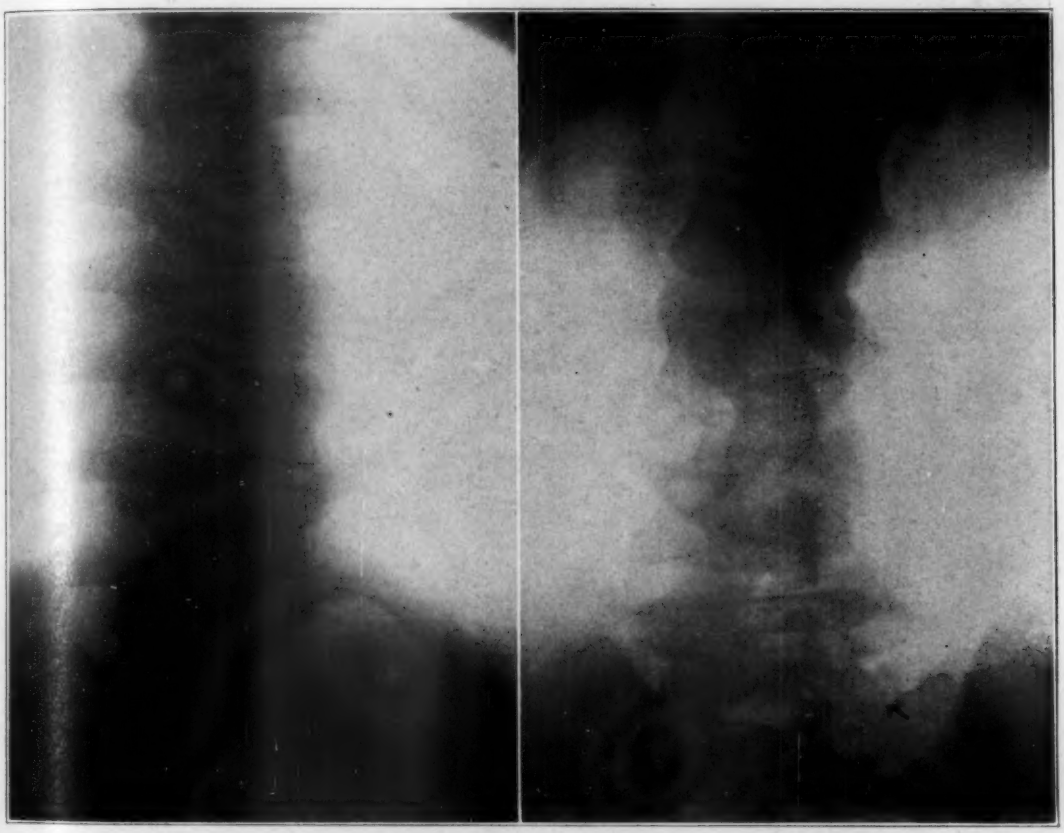

Fig. 6.—Appearance of the spine in an early case of dorsal curvature to right. Left: Curve in the dorsal region; right: changes in the articulation of sacro-lumbar region on the right side.

3. It is the loss of muscular balance between the two sides of the lumbar caused by the change of shape of the last lumbar which is embarrassing the spinal column in the lumbar region. The action of the erector spinae, on the convex side, trying to resist the bending of the lumbar vertebrae over to the other side, and resisting the pulling of the quadratus lumborum and the multifides of the side of the spine,

where the thickening of the last lumbar vertebra takes place, accounts for the widening of the intervertebral spaces on the convex side of the lumbar curve, and the approximation of the intervertebral parts on the concave side, which is usually found to a marked degree in the lumbar region and to a milder degree in the lower three or four dorsal, and is practically absent in the upper nine dorsal bodies.

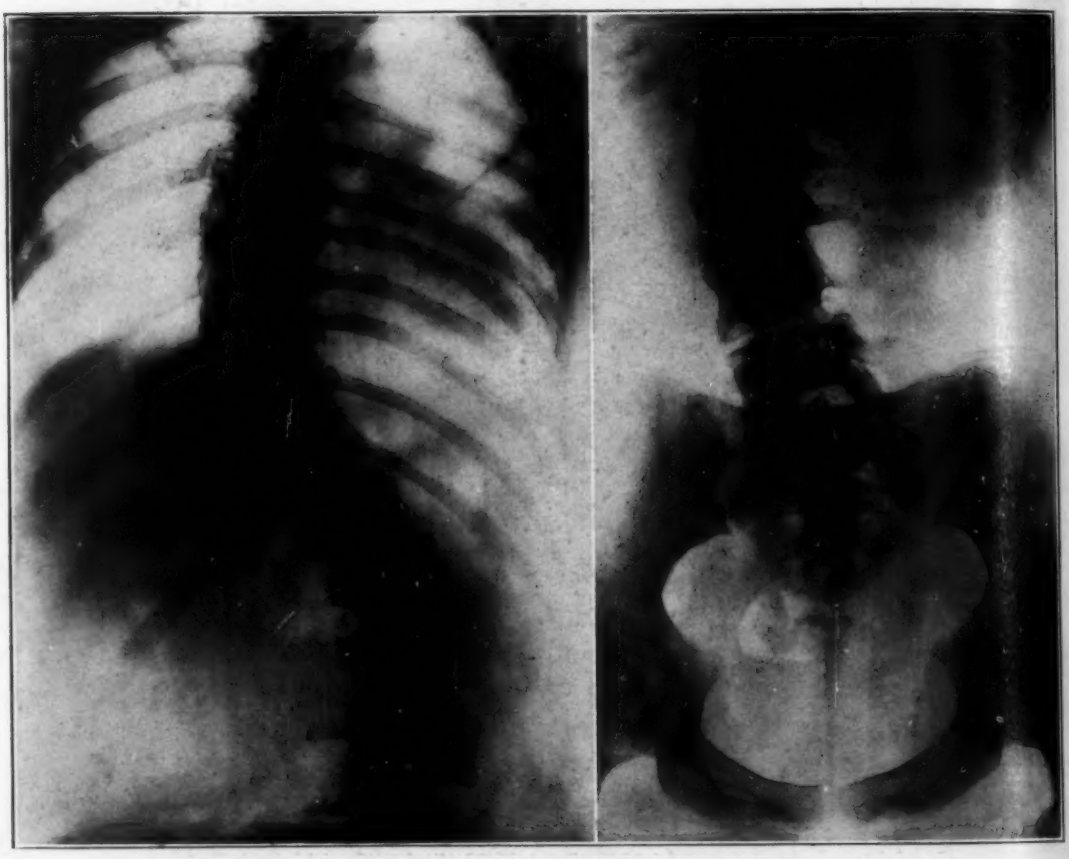

Fig. 7.—Appearance of spine of girl, aged 17 years, who had marked lateral curvature. Left: Wide separation of the interspaces on the convex side of the curve in the lumbar region; right: hypertrophic appearance of the lumbosacral junction on the concave side.

4. When the patient suffering from a curvature is placed on a stretching table, in supine position, and fully relaxed, the curvature will yield to a stretch from above and below, provided enough force is applied, which usually is from 25 to 30 pounds. A roentgenogram taken in that corrected position will show that the correction of the

curve has taken place through the approximation of the widened intervertebral surfaces of the lumbar. If the stretch is applied from one end of the body only, the most corrective results can be obtained by stretching the patient from below, and anchoring the head from above, rather than by using the head stretch alone (Figs. 8 and 9).

Fig. 8 (Miss R., aged 25).—Marked case of rotary lateral curvature showing all the ear marks of a long standing affection, including wedging of the ninth and tenth dorsal vertebrae.

5. Roentgenograms taken of patients suffering from curvature with their supposedly corrective corsets on do not show any appreciable alteration or improvement in the spinal column, unless the stretching is applied at the same time.

Fig. 9 (Patient shown in Figure 8).—The roentgenogram was taken while the patient was being stretched on the stretching table from above and below. The spine is attempting to straighten by approximation of the lumbar vertebrae at the convexity.

6. Visible and palpable deformities of the spine, seemingly slight, do not always indicate the real extent of the deformity as found when studied by means of roentgenography; and many cases which show improvement after treatment may be misleading unless one enlists the aid of the roentgen rays.

7. The study of the electrical reactions of the muscles of the spinal column is most essential, in order to determine the mode of treatment to be instituted in cases of curvature, especially in early cases. Hypo-excitability of muscles shows fatigue of such muscles and their need of rest and strengthening, by keeping the patient in a relaxed posture, instead of aggravating the condition by gymnastics. On the other hand, hyperexcitability of a group of muscles should be treated by immobilization in a position that would relax those muscles.

In many cases that I have seen in which there was at first a very slight curve, a markedly crippled spine has been the final outcome because the foregoing rules were not heeded.

It is indeed interesting to observe that, in the majority of cases of curvature, there seems to be hyperexcitability of the muscles on the convex side of the curve; while the concave side will stand three or four times the amount of electric stimulation before reaction sets in. In the lumbar region, the hypo-excitability of the muscles on the concave side seem to be much more marked.

It appears, then, that in the sacrolumbar portion of the spine we find the most important cause for curvatures; also that even in those curves which to the eye seem only in the dorsal region it will, in the majority of cases, be found that the last lumbar vertebra is the original source of the trouble, and also that muscular irritability and fatigue of some groups in the lumbar region are another source of deformities in the spine. The question naturally arises: How can we explain the foregoing phenomena? In view of the fact that the lower part of the spine is that part of the column which bears the greatest burden in the maintenance of the proper equilibrium of the body in the erect posture, that locality is supplied with powerful muscles which act as extensors when both sides act equally. The constant addition to the body weight as a result of growth must perforce add an additional burden to those muscles, which must be met by the power of growth inherent in the muscles; and since that region demands so much of the growth of the muscles, it is here the vulnerablity to feebleness of growth, caused either by systemic toxemias or other conditions, will be most marked, especially in early childhood, when the patient first assumes a constant and permanent erect posture. It will then depend on the number of muscles involved in this feebleness; also whether one side or both sides of the lower muscles of the spine are involved.

In speaking of bone formation and growth, Dr. Murk Jansen [15] points out the following valuable facts:

As soon as side pressure adopts the character of muscle function, bone tissue is formed in the direction of pressure, either detached from the bone in the form of bones lying in the tendons (sesamoid bones), or connected with the bones in the form of prominences (tuberosities, trochanters). The jerky

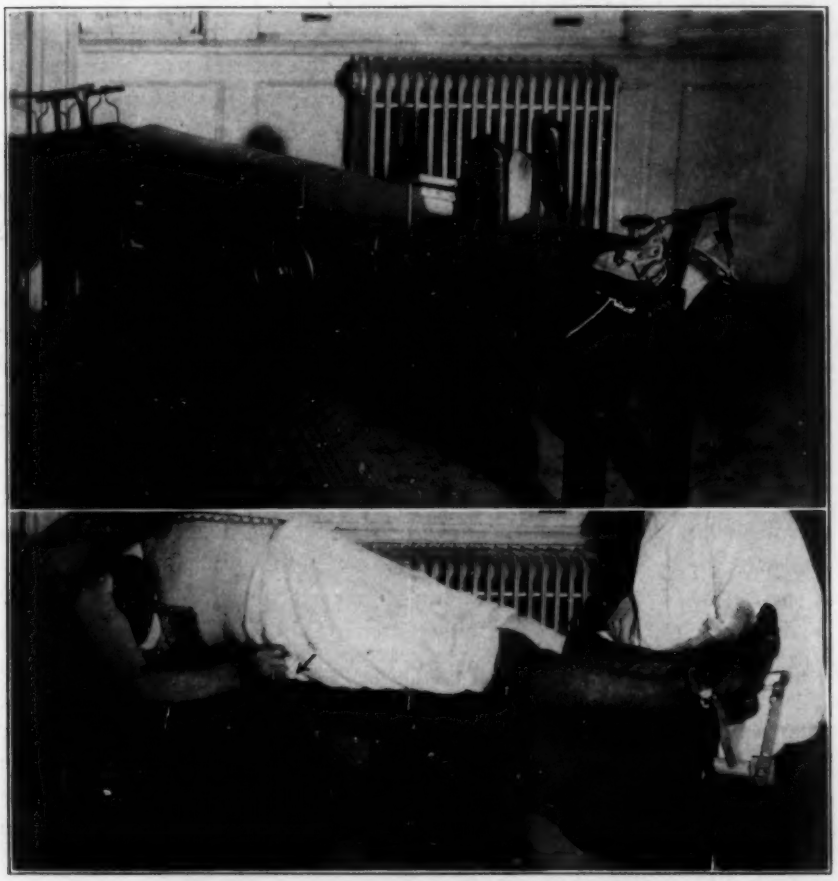

Fig. 10.—Above: Extension table. The head is at the right. Below: Patient on extension table. The amount of stretching can be regulated by the patient by manipulation of a crank.

pressure of muscles in connection with that of gravity appears to be the mechanical stimulus which promotes bone formation, at least in the bones of the extremities and the vertebral bodies.

15. Jansen, Murk: On Bone Formation, New York, Longmans, Green & Company, 1920, pp. 78-80.

Not only in the form but in the size of bones, the jerking pressure of muscle action and gravity seems to have an effect. There is an unmistakable parallelism between the intensity of that pressure and the length of the extremities, and their parts both in animals and in man. . . . Certain it is that not in the jerking pressure of muscle action and gravity as such, but rather in the pressure of function—functional pressure—the stimulus for bone formation in the various skeletal parts is to be traced.

It is therefore in the lumbosacral region that the two curves meet, the lordotic of the lumbar and the kyphotic of the sacral, also that the freely movable lumbar meets with the immovable sacrum, and the jerking pressure of muscles and gravity are greatest; and the last lumbar will necessarily bear the brunt of these opposing pulls, and stresses. The growth of its body and of its component parts will therefore be greatly determined by that pull, as well as by the functional stress and pressure of the muscles in its immediate vicinity, with a resultant deformity in the spinal column as it is attempting to readjust itself.

In the male, provided the deformity is not very marked, as the growth of the bones of the vertebrae go on, the sacrum enlarges, forming a broader base, and a greater forward angle with the last lumbar. Thus, there is a tendency for the deformity in the spine to be called to a halt. In the female, as a result of further changes which take place in the sacrolumbar junction and pelvis, even after the advent of puberty and adolescence, gravity is further threatened and constant readjustment must go on, in order to keep the body erect; hence the increase of the deformity, unless intelligently treated.

CONCLUSIONS AND CLINICAL APPLICATIONS

1. The size and thickness of the intervertebral cartilages or disks are in close relationship to, and developed in accordance with, the amount and extent of mobility of the spine. The dorsal vertebrae, having limited motion, have the smallest disks; while the cervical and the lumbar, with their free motility, have the larger. Such intervertebral cartilage will, therefore, diminish in size and thickness when, through operative procedures, such free motility is interfered with, or entirely abolished.

2. The intervertebral disks act as shock absorbers, or buffers, and diminish the jarring of the vertebrae produced in walking, also preventing the jarring of the steps taken from being transmitted to the head. The latter function is further helped by the natural curves assumed by the spinal column. Hence, any diminution of the size of the intervertebral cartilages is bound to have a telling effect on the welfare of the body as a whole, through its irritating effect on the nervous system.

3. The mobility of the dorsal spine (except the three lower dorsal) is practically limited to rotation about the more movable parts of the

spinal column, i. e., the cervical and lumbar vertebrae, and hence any operative procedure designed to prevent or overcome further rotation is bound to be a failure, unless the lumbar is anchored at the same time, owing to the latter's limited rotation, and both the dorsal and the lumbar are made immobile by attaching the entire immobile column to the sacrum.

4. Free mobility of the lumbar spine is essential to the welfare of the human body; first, on account of its large intervertebral disks mentioned above, and also on account of the direct connection of the bodies of the vertebrae of that region, as well as its ligaments, with the sympathetic nervous system, through the direct supply of the sympathetic nerve filaments to that region, in addition to the usual supply of communicantes. Such mobility should therefore not be interfered with without weighty indications for such a procedure.

5. The free sympathetic nerve supply to the lumbar spine, and the latter's intimate connection with the internal organs resulting from this supply may account for the far-reaching effects resulting from seemingly slight injuries in that region, especially in women, and should be thought of by the physician in interpreting symptoms, especially so when the symptoms are out of proportion with visible signs.

6. The clinical and prognostic significance of the free mobility of the various parts constituting the lumbar spine lies in the fact that injuries of the upper lumbar, although followed by ankylosis in that region, will have a temporary crippling effect only on the mobility of the entire lumbar region; because, as soon as healing and cessation of pain will permit, the lower portion of the lumbar spine will resume its normal motion, and compensate for the loss of function of the upper part.

7. The muscular system of the back plays an important part in the causation of deformities of the spine, influencing the shape and form of the vertebral bodies as well. Therefore, those muscles should be studied carefully as to their present condition, for the presence of hyperexcitability or hypo-excitability, temporary fatigue or permanent damage, and also for other probable underlying causative factors, before one is in a position to determine whether or not the patient is in need of rest in recumbency or immobilization of the part affected; or in need of a course of calisthenics.

8. In view of the fact that the majority of curvatures of the spine have their origin in the lower part of the lumbar vertebrae at the junction of the sacrolumbar, a roentgen-ray examination of the spine for such a deformity is useless, unless it takes in the region mentioned (properly focused), even though the physical examination does not warrant such inclusion.

9. Plaster corsets per se do not seem to have the power of correcting a curvature of the spine unless accompanied by longitudinal extension and counterextension. Lateral pressure and counter pressure alone does not seem to have the desired effect. This observation is corroborated by roentgenograms taken through the plaster corset with the patient in recumbent posture.

10. Temporary correction of a curvature, even in the dorsal region, seems to take place through the approximation of the widened intervertebral spaces on the convex side of the lumbar region. The correction is further facilitated by placing the patient on the extension table in a supine position (rather than prone). In that position, all the muscles of the back seem to relax, and yield better to longitudinal stretching from above and below to the point of toleration. Roentgenograms taken of the patient's spine in that position show the greatest amount of correction, with the least amount of inconvenience. It therefore seems reasonable to assume that a jacket applied while the patient is in that position with proper extension should be most effective in the correction (Fig. 10).

CHILLS OCCURRING EARLY IN APPENDICITIS BEFORE OPERATION AND THEIR INDICATION OF AN OPERABLE STAGE OF PYLEPHLEBITIS *

WILLIAM THALHIMER, M.D.
MILWAUKEE

Gerster,[1] twenty years ago, made the following statements:

It seems clear that, as regards purulent pylephlibitis caused by appendicitis, an early diagnosis of the primary trouble and prompt operation offer the only reliable safeguards.

The occurrence of a chill is of the gravest import and should be considered to constitute a more urgent indication to operate than even the signs of local peritonitis. Where much necrosis is found, it would be very desirable to expose and evacuate thrombosed veins.

The evacuation of septic thrombi from the jugular vein in mastoid disease has yielded such excellent results that the application of the principle to the portal vein would be natural and logical.

Gerster's observations in his series of cases definitely proved his point, and in another series to be presented here it will be proved again, with the addition of convincing studies of the pathologic anatomy of pylephlebitis secondary to appendicitis.

It should not be necessary to make this study a second time, but the pioneer teaching of Gerster has been so completely neglected in all works on appendicitis and in the present day surgical treatment of this disease that this communication is made with the hope of recalling the truth and tremendous importance of his original observations.

The principles quoted above were practiced on the service of Dr. Gerster and were impressed on me during my internship (1908-1910). It was from Dr. A. A. Berg, one of the surgeons on the service, that I learned most about these methods, and owing to his kindness, I had the privilege of studying all of the cases reported here (except one), while I was associated with him from 1911 to 1918.

The term pylephlebitis is usually used to indicate an infected thrombophlebitis of the portal system. Its commonest cause is acute appendicitis, but any septic process of the gastro-intestinal tract may be the cause, such as ulcerated carcinoma, chronic ulcerative colitis and sigmoid diverticulitis.

---

* From Columbia Hospital.

1. Gerster, A. G.: On Septic Thrombosis of the Roots of the Portal Vein in Appendicitis and on Pylephlebitis, Together with Some Remarks on Peritoneal Sepsis, Tr. Am. Surgeon's Assn. **21**:39, 1903.

The thrombosis begins in the small radicles of the portal vein, and usually extends by continuity until the main trunk is reached. It next proceeds into the intrahepatic radicles and in the liver causes extensive periphlebitis and great numbers of liver abscesses. In some cases, emboli undoubtedly detach themselves when only small branches of the portal system are involved, and lodge in the liver before the process of thrombosis has reached there by direct extension in the veins. It is interesting to note that, whereas an infected thrombosis of the veins of the general circulation (of the sigmoid sinus after mastoid disease, or of the ovarian veins in postpartum infection) is accompanied by a bacteriemia and blood cultures are positive, pylephlebitis does not cause bacteria to appear in the general circulation, and blood cultures are negative. Undoubtedly, the organisms are filtered out by the liver. Under only one circumstance will blood cultures be positive in cases of pylephlebitis, and that is late in the disease when the liver abscesses cause an infective thrombophlebitis of the branches of the hepatic veins, just as appendicitis caused the pylephlebitis originally. Bacteria then appear in the general circulation, for the lungs do not act as an efficient filter. As a rule, sizeable emboli from the hepatic veins soon lodge in the lungs and cause pulmonary abscesses.

Usually, pylephlebitis manifests itself from several days to several weeks after the onset of appendicitis, whether appendectomy has been performed or not. By this time, the pylephlebitis is well advanced; and it is generally a fatal complication. However, a number of cases of recovery are reported. Some of these are well authenticated, but others because of the nature of the disease, cannot be considered as proved.[2]

Usually by the time pylephlebitis is recognized, the prognosis is fatal, even though a patient occasionally recovers. Since in most cases of acute appendicitis today, operation is performed as soon as the case is diagnosed, pylephlebitis is generally placed among the postoperative complications. It is intended, by the data presented below, to demonstrate that in some patients pylephlebitis has already developed by the time the appendectomy is performed, but is at an operable, curable stage. This can be recognized by the clinical course of the case and by finding thrombi in the veins of the mesentery of the appendix and in those which drain these veins at the operation.

Pylephlebitis, as a postoperative complication, has been well described. It may follow any variety of acute appendicitis, from an apparently mild attack to one associated with perforation with localized or general peritoneal involvement. It usually occurs in cases in which

2. Reference to important bibliography and to cases of pylephlebitis with recovery will be found in an interesting article by Frederick Christopher, "Pylephlebitis of Appendiceal Origin, Simulating Lung Abscess," Surg. Clin. N. America, August, 1921, p. 1093.

the appendix is red, turgid and edematous and its mesentery likewise. As a rule, the patient's postoperative temperature does not fall to normal, as it generally does in a few days, but remains constantly elevated or fluctuates. The most significant symptom is the occurrence of chills with a high temperature. Soon after these, slight jaundice appears, which rapidly intensifies, owing to involvement of the liver, which becomes enlarged and tender. With these symptoms, general, irregular and very severe abdominal pain occurs. The course after this is downhill, but usually not very rapid, death supervening, as a general rule, weeks afterward.

It should be emphasized that the most significant symptoms of the postoperative development of pylephlebitis is the onset of one or more chills. The principle which I wish to stress is that a chill during an attack of appendicitis occurring before operation is just as indicative of pylephlebitis as a postoperative chill. The suppurative thrombophlebitis will be in its incipient stage at the time of the original operation, and, if looked for and recognized, can be eradicated by a comparatively few additional measures in the ordinary operation of appendectomy, which will be described below; and cure is more likely to follow than if the warning given by the preoperative chill is neglected and merely the appendix is removed. The reason why pylephlebitis does not always develop following simple removal of the appendix will be discussed below.

SIGNIFICANCE OF CHILLS DURING AN INFECTION

The exact cause of chills during an infection is not known. Evidence is accumulating to indicate that there is an intimate relationship between the development of septic, or even aseptic, thrombi, and chills. For example, chills occur in practically all cases of thrombosis of the sigmoid sinus in mastoid disease or of the ovarian or uterine veins in postpartum infection, and in cases of subacute vegetative endocarditis, the lesions of which are really septic thrombi on the heart valves. There are instances in which this relationship is not so clear; such as chills during pyelitis, cystitis and pneumonia. The important point to be borne in mind here is that chills follow thrombosis of small and large vessels, especially those of the venous system.

ORIGIN OF PYLEPHLEBITIS FROM APPENDICITIS

Gerster [1] noted the presence of thrombi in the veins of the mesentery of the appendix and in the regional small veins into which these empty, in a number of cases of appendicitis with chills. When one considers the pathologic anatomy in acute appendicitis, it is remarkable that thrombosis of these small veins does not occur oftener. These veins lead into the ileocolic vein, which is a tributary, through the

superior mesenteric vein, to the portal vein. So much of the portal system is involved in cases of pylephlebitis which come to necropsy that the origin of the process in these small veins cannot be determined. The cases reported below furnished an opportunity to study the beginning of pylephlebitis secondary to appendicitis. Aschoff [3] has described this also, and his description of this and of the pathology of acute appendicitis is so illuminating that it is presented almost verbatim.

He says:

> Death of the tissues of the appendix may be caused by the energetic action of bacteria which gain entrance to these tissues; for example, through an acute ulcerative appendicitis. Necrosis of the wall of the appendix is the commonest complication of the ulcerative stage, and is the result of either anemic or hemorrhagic infarction. The infarction is the result of loss of circulation of the wall of the appendix, due either to arterial or to venous thrombi. If this process extends to the large vessels of the mesentery of the appendix necrosis of the entire appendix may result. The blood supply of the wall of the appendix nearest the mesentery is poorer than that elsewhere. Therefore, this portion of the appendix is more susceptible to extensive infection than other portions. Infection at this location is more likely to extend deeply into the mesentery of the appendix and cause thrombosis of its blood vessels. The infected thrombophlebitis may proceed by direct extension into the superior mesenteric vein, then into the portal vein and finally into the liver.

The fact that this thrombotic process has not extended beyond the wall of the appendix by the time most diseased appendixes are removed probably accounts for the infrequency of pylephlebitis after appendectomy.

It seems remarkable that one finds practically no observations recorded about these early cases of septic thrombophlebitis of the small veins of the appendix and its mesentery (mesenteriolum), besides those of Gerster [1] and of Aschoff.[3] So far as known, no one has demonstrated bacteria in these early thrombi, as will be demonstrated in the cases to be reported here. Therefore, until now these cases have not been proved to be early cases of septic pylephlebitis.

SURGICAL TREATMENT OF CASES OF APPENDICITIS ACCOMPANIED BY CHILLS

Few logical suggestions for the treatment of advanced pylephlebitis have been made and these have been applied only a few times. Wilms,[4] after four days of chills in one patient, ligated the ileocolic vein beyond the portion containing suppurating thrombi, but did not excise the

3. Aschoff: Die Wurmfortsatzentzundung. Jena, Gustav Fischer, 1908.

4. Wilms: Centralbl. f. Chir., 1909, No. 30, p. 104; abstr. Prog. Med., June, 1911, p. 135.

involved veins. Chills did not recur, and the patient recovered. Braun [5] has successfully performed the same operation twice. He had to ligate the ileocolic vein higher up; i. e., nearer the main trunk of the portal vein, because of more extensive involvement, and in one case he resected 8 cm. of the vein plugged with suppurating thrombi. In one case, jaundice and enlargement of the liver gradually subsided, showing that even in the presence of these later changes, if the feeding focus in the vein below is removed in time, fatal septic portal thrombosis and liver abscesses can be prevented.

Aside from the results just quoted, it must be perfectly clear that the circulation is already obstructed in these thrombosed veins, and the chances of infarction of the intestines are not increased by ligation of the veins already clogged with thrombi, as is proved by these successful cases. On this basis, Neuhof [6] has suggested ligating the portal vein itself in advanced pylephlebitis. He did this successfully in dogs by a method of gradual ligation. As far as is known, there have been no cases published in which this has been done in man, although the procedure should undoubtedly be tried in otherwise hopeless cases of pylephlebitis.

Since it is believed that chills have a serious significance in acute appendicitis, patients should not be relied on to volunteer a history of chills, but should be questioned particularly about this symptom. With a history of one or more chills, operation should be performed immediately, even though the other symptoms do not indicate urgency.

A lower right rectus or a Kammerer incision permits easy enlargement, while the size of the muscle splitting, or McBurney incision, is self-limited, and so is contraindicated.

In exposing the appendix, care should be taken to handle it and the ileocecal region gently, so as not to dislodge any thrombi which may be present. Sometimes, it is possible to detect thrombosed veins by inspection alone. The mesentery should be cut through as close to the base of the appendix as possible, and this should be done slowly and deliberately, without first applying clamps, in order to determine whether the vessels are patent and bleed. Bleeding points are caught. Both cut surfaces of the mesenteriolum should be carefully inspected for thrombosed veins. If none are found, it is safe to complete the appendectomy in a routine manner.

If thrombi are found, all veins in the mesentery of the ileum at the ileocecal junction and those of the caput coli must be carefully examined. Next, the ileocolic vein should be examined (this will require an

5. Braun: Beitr. z. klin. Chir. **86**:314, No. 2, 1913, abstr. Prog. Med., June, 1914, p. 136.

6. Neuhof, H.: Surg. Gynec. & Obst. **16**:481, 1913.

enlarged abdominal incision). This can be done in one of two ways. The small intestines can be carefully packed away above and toward the midline, exposing the posterior parietal peritoneum. The ileocolic vein extends upward and slightly toward the midline, beginning immediately at the angle formed by the ileum and cecum. It is directly beneath the peritoneum and can easily be seen and identified. If it is palpated, this should be done gently. By splitting the overlying peritoneum, it can be satisfactorily exposed. Another method is to mobilize the cecum and ascending colon by incising the parietal peritoneum along the outer side and, by gentle blunt dissection toward the midline beneath these structures, lift them up and reflect them mesially. This is an easy and safe procedure, and in addition to being gentle, one must be careful not to lift up the right ureter along with the peritoneum. The ileocecal and contributary veins can then be approached from the rear.

With either method of approach, all small veins suspected of being thrombosed should be nicked to determine whether they will bleed. If patent, they can be easily caught and ligated; if thrombosed, it is preferable to excise them after ligating beyond, although they may be incised and the thrombi evacuated, as suggested by Gerster, or ligation above the thrombi may be sufficient. These same rules hold for larger veins, even for the ileocolic vein itself. The appendix is removed whenever convenient during the operation, and general rules for drainage are followed.

Therefore, it follows that every case of acute appendicitis should be considered as a potential one of early pylephlebitis, whether there is a history of chills or not. Consequently, the appendix and its neighborhood should always be carefully inspected (at operation) for the presence of small thrombosed veins, so that these can be dealt with. The type of appendicitis in which they most commonly occur and are most likely to be overlooked are those in which there are acutely inflamed, large red edematous, turgid appendixes, whose mesenteriolums are likewise edematous.

Four cases of acute appendicitis accompanied by one or more chills were studied. In all four cases, bacteria containing thrombi were found in the veins of the mesentery of the appendix. Three patients were submitted to the operation described above, and the thrombophlebitic process was apparently checked; for no further chills or untoward symptoms occurred, and recovery was uneventful. In the fourth case, the appendix was submitted to me for examination after it was removed, and thrombi were found on gross and microscopic examination. A secondary operation was recommended for removal of the thrombosed veins, but permission for this was refused by the parents of the patient, a boy, 16 years old. The temperature did not return to normal; further chills developed, and the case ran a typical course of pylephlebitis, with

jaundice, enlarged tender liver, liver abscesses, some of which subsequently were drained; and finally, pulmonary abscesses, exhaustion and death.

REPORT OF CASES

CASE 1.—*History.*—A woman, aged 26, who had been sick for two days with symptoms of bronchitis, on the day of admission had a severe chill with rise of temperature to 103.4 F. There had been vague abdominal cramps, but no vomiting or diarrhea.

Physical Examination.—There was slight tenderness in the right iliac fossa, but no muscle spasm. Along the flare of the right ilium, just above the brim of the true pelvis, a small slightly tender mass, about 2 by 5 cm., was felt.

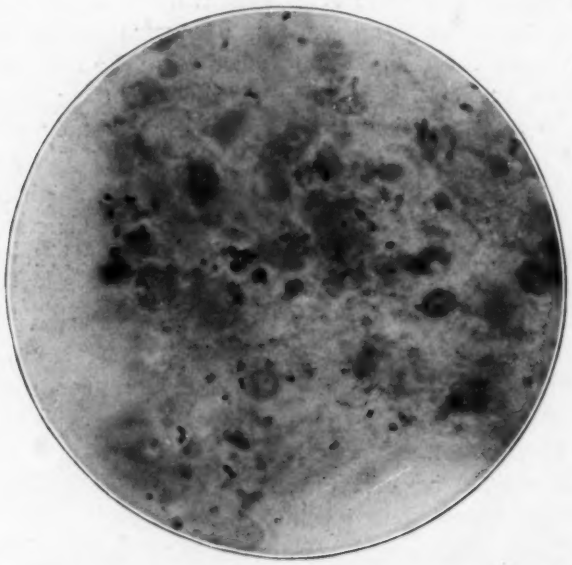

Fig. 1.—Bacteria in thrombus in vein of mesenteriolum (Gram-Weigert stain; × 1200).

Operation (Dr. A. A. Berg, Feb. 22, 1914).—A right rectus incision was made, and the appendix was found at the location of the mass which had been felt. It was slightly adherent by fibrin to the peritoneum of the pelvic wall. The appendix was gently freed. It was 2 cm. in diameter, the mesenteriolum being equally thick. Both were much reddened and edematous. The mensenteriolum was carefully incised as close to its root as possible. Bleeding occurred in spurts from the artery but not elsewhere on the cut surfaces. The veins were filled with dark red and purulent thrombi (Fig. 4).

The abdominal incision was then enlarged, and the reflection of the peritoneum of the caput coli onto the lateral abdominal wall was incised. The caput was then lifted up, and the peritoneum around the base of the appendix was dissected upward and removed for a distance of 2 cm. Several suspicious looking veins about this region were cut into, but all of them bled freely. Hemostasis was established. The ileocolic vein was soft and contained no

thrombi. The appendix was removed in the usual manner. A rubber drainage tube was placed, down to the appendix stump, and the abdomen closed in layers as usual.

Course.—Convalescence was uneventful. The temperature became normal in several days, and the patient was discharged in twenty days.

Gross Appearance.—In addition to the appearance as described above, the mucosa was found gangrenous.

Microscopic Examination.—All of the coats of the appendix showed marked edema, congestion and leukocytic infiltration, and the mucosa showed practically complete necrosis. The acute inflammatory process was found in the mesenteriolum, several of the larger veins of which were filled with purulent thrombi

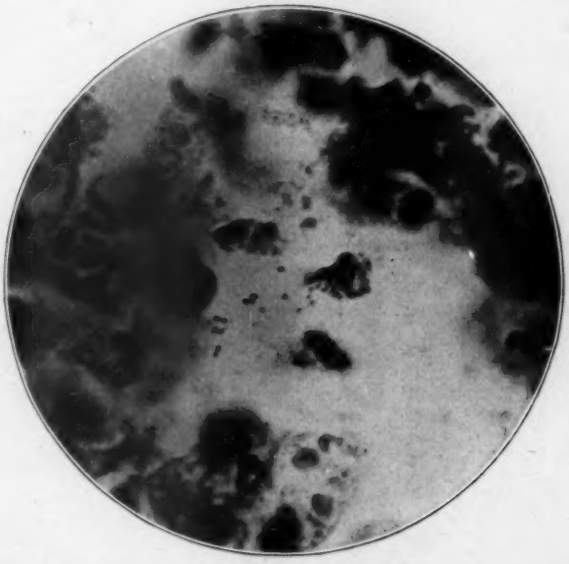

Fig. 2.—Bacteria in thrombus in vein of mesenteriolum (Gram-Weigert stain; × 1200).

(Fig. 4), in which were present many cocci, as demonstrated by both Gram-Weigert and giemsa stains (Fig. 1). Cocci were also found in the submucosa, muscularis and serosa, and here and there in the mesenteriolum, as well as in the veins just described.

Case 2.—*History.*—A boy, aged 8 years, had been suffering about twenty-four hours with pain in the abdomen. The temperature rapidly rose to over 103 F., with several attacks of vomiting, and severe chills.

Physical Examination.—There was generalized and marked abdominal rigidity and tenderness.

Operation (Dr. A. A. Berg).—An appendix which was almost all gangrenous but not perforated was found, covered with a greenish yellow fibrinous exudate. The veins of the root of the mesenteriolum bled when incised. Nevertheless, the peritoneum was dissected away for a distance of 3 cm. around the base of the appendix. The appendix was removed, a rubber drainage tube was inserted and the abdominal incision was closed.

Convalescence.—This was uneventful.

Microscopic Examination.—The mucosa was gangrenous, as were also portions of the serosa. The wall showed acute inflammation and many miliary abscesses. Many small veins of the appendix wall and of the mesenteriolum were

Fig. 3.—Thrombus in vein of mesenteriolum. The thrombus is lamellated in one place, and purulent elsewhere (hematoxylin and eosin stain; × 400).

lined with pus cells embedded in hyaline material (early thrombi) and some were filled with pus cells (purulent thrombi). Bacteria, both cocci and bacilli, were present in great numbers throughout the appendix and mesenteriolum, and a few were found within the thrombosed veins. The bacilli were revealed only

by the giemsa stain, the cocci by both this stain and the Gram-Weigert, the bacilli being therefore gram-negative.

CASE 3.—*History.*—A man, aged 32, had been ill for four days with a typical attack of appendicitis, and a severe chill occurred four hours before operation.

Operation (Dr. A. A. Berg).—The appendix was gangrenous, but not perforated, with marked edema of the mesenteriolum. Thrombi were evident

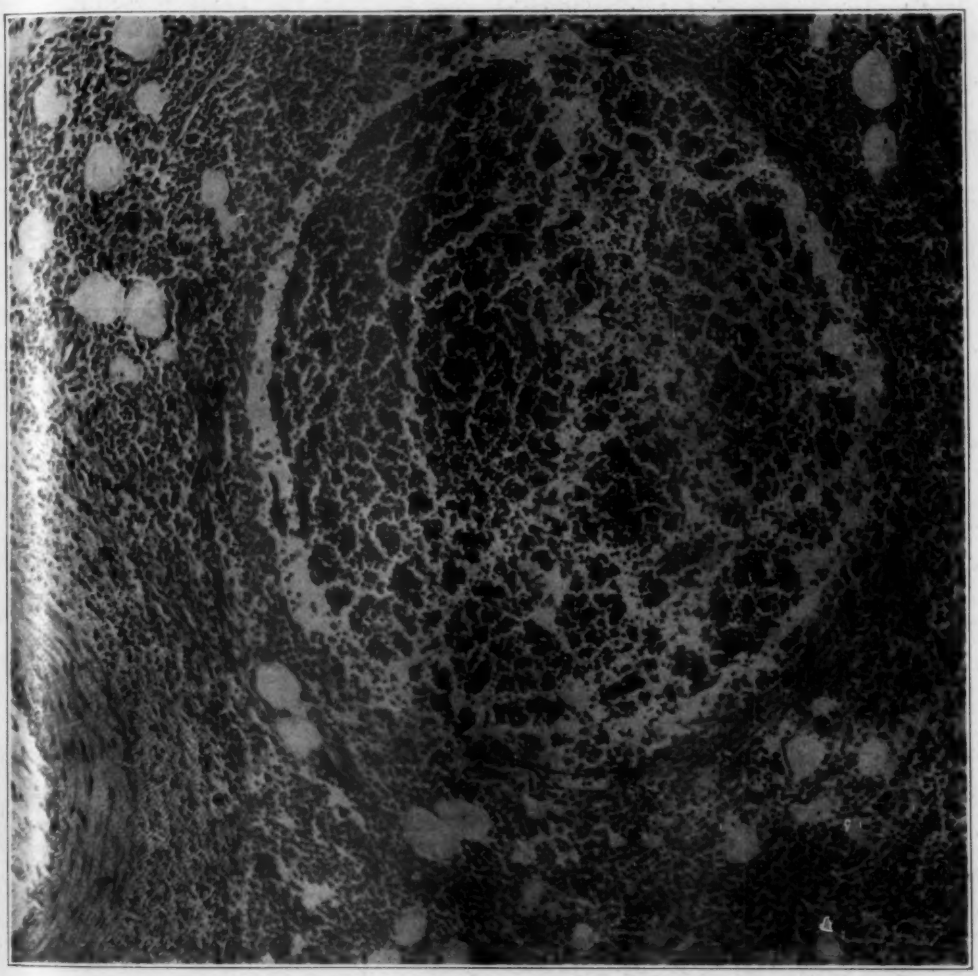

Fig. 4.—Purulent thrombus in vein of mesenteriolum (hematoxylin and eosin stain; ×400).

grossly in the mesenteriolum when this was incised. The operation was completed, and the appendix was removed in the same manner as in the two operations reported above.

Convalescence.—This was uneventful.

Microscopic Examination.—Necrotic areas were present in the appendix and there were changes of acute inflammation in it and in the mesenteriolum. Many

small veins of the mesenteriolum were filled with purulent thrombi, which contained cocci, demonstrated with the Gram-Weigert stain. Cocci were also present in the wall of the appendix and in purulent areas in the mesenteriolum.

CASE 4.—*History.*—A colored boy, aged 16 years, five days previously was suddenly taken with severe pain in the abdomen, and became nauseated and vomited. This had continued and the night before he was first seen and brought to the hospital he had a severe chill.

Operation (Dr. P. H. McGovern).—The appendix was found retrocecal, sharply curved on itself and adherent. The adhesions were freed, and the red edematous appendix was removed by the usual method. Drainage was not done. The abdomen was closed in layers.

Microscopic Examination.—There was marked edema and leukocytic infiltration of all the coats of the appendix and of the mesenteriolum. The mucosa was necrotic. The veins of the mesenteriolum were filled with thrombi, parts of which were purulent, the other portions mixed, red and gray, lamellated thrombi (Fig. 3). Large numbers of cocci were found with the Gram-Weigert stain in the thrombi (Fig. 2) and in the tissues of the mesenteriolum and submucosa of the appendix.

Postoperative Course.—Because of the findings, a secondary operation was advised the next day in order to eradicate the thrombotic process. The boy's parents, however, refused to permit any further operation. The temperature remained high, varying from 102 to 103 F., and three days after operation a chill occurred. The liver soon became enlarged and tender, jaundice developed and chills occurred at irregular periods. The wound healed by first intention. The patient was taken home after six weeks, at which time he presented a typical picture of pylephlebitis. He was brought back to the hospital three weeks later, with marked enlargement of the left lobe of the liver. Through a small abdominal incision several large liver abscesses were drained. This process appeared to be confined to the left lobe. Liver material evacuated with the pus at the operation, on microscopic examination, showed many small veins filled with purulent thrombi.

For a while the patient improved, but later, after he again left the hospital, he developed a purulent foul expectoration, bringing up large amounts of sputum, and died several weeks later, about four months after the onset. No necropsy could be obtained.

A STUDY OF MAGNESIUM WIRE AS AN ABSORBABLE SUTURE AND LIGATURE MATERIAL*

M. G. SEELIG, M.D.

ST. LOUIS

Considering the remarkable progress that has been made in the purely technical development of surgery, there has been a strikingly small advance in the preparation of suture and ligature material. This is not due to the fact that our present material is satisfactory; quite the reverse. Silk and all other nonabsorbable material frequently act as foreign bodies; whereas, catgut is at best an uncertain quantity as regards its sterility, its calculable absorption time and its rôle as a tissue irritant. The essential reason for the universal use of silk and catgut is that, with all their disadvantages, they are superior to all other known materials.

The ideal suture is soft and pliable as silk, causes the slightest possible tissue reaction, possesses adequate tensile strength and has a definitely calculable absorption time, varying, with the caliber of the suture, from a few hours up to weeks.

Although magnesium is a highly absorbable metal, it has received comparatively scant attention from surgeons. Payr,[1] Chlumpsky,[2] Lespinasse[3] and Andrews[4] have furnished the only reports in the literature, dealing with this metal as an aid in wound closure. The work of Payr, Chlumpsky and Lespinasse deals exclusively with magnesium prostheses in the anastomosis of blood vessels and intestines. Andrews directs his attention to the question of magnesium as a substitute for other ligatures and sutures in wound closure. None of this work is fundamental in character, and it develops nothing of importance other than that the metal is absorbable, that in the process of absorption, hydrogen gas is evolved and magnesium oxid is formed, and that no demonstrable harm is done to the tissues. Lespinasse states

---

* This study has been fostered by a grant from the Fenger Fund, Chicago.

* From the Department of Surgery of Washington University School of Medicine.

1. Payr, E.: Weitere Mitt. u. Verwendung d. Mag. bei. d. Naht. d. Blutgefaesse, Arch. f. klin. chir. **64**:726, 1901.

2. Chlumpsky: Beitr. z. Darmknopffrage, Mitt. a. d. Grenz. d. med. u. chir. **3**:416, 1907 (Supplementary volume).

3. Lespinasse, U. D.; Fisher, G. C., and Eisenstaedt, J.: A Practical Mechanical Method of End to End Anastomosis of Blood Vessels, J. A. M. A. **55**:1785 (Nov. 19) 1923.

4. Andrews, E. W.: Absorbable Metal Clips as Substitutes for Ligatures and Deep Sutures, J. A. M. A. **69**:278 (July 28) 1917.

that the hydrogen is absorbed almost as fast as it is evolved, a statement at variance with our experience. Payr and Chlumpsky show that even microscopically no harm is suffered by tissue as delicate as vascular endothelium. Andrews carefully measured the absorption time of magnesium (as well as of aluminiun, cadmium and zinc), and studied the effect of magnesium and its alloys on the tissues. He came to the conclusions that "the efforts to make an ideal alloy are encouraging, but not wholly successful," and that "the physical properties of magnesium do not recommend it for any use demanding tensile strength." Andrews found that all his alloys were "of a pasty consistence, like soft solder, when half melted, and had all the bad properties we wished to avoid." Further, he found that magnesium wire "cannot be tied even in loose knots, as it breaks immediately on kinking, and it cannot be twisted even loosely, without showing its brittle nature." [5]

Here, then, were a group of studies demonstrating that magnesium possessed one very valuable physical property (absorbability) and some very disappointing properties, as far as ligature material is concerned.

The object of our study is to check up the question of absorbability of the metal and then to see whether the brittleness and poor tensile strength of the metal can be modified into suitable ligature and suture material, just as Tungsten has been modified to adapt it for use as an incandescent filament.

Andrews' observation regarding the brittleness of magnesium we found to hold true for magnesium wire obtained in the open market from various agencies. The statement that the metal was absorbable we also found true. The rate of absorption we were able to check up very simply by planting short lengths of magnesium wire subcutaneously in the ears of rabbits and noting in roentgenograms the rate of absorption. A piece of magnesium wire 1 cm. long and of 0.05 inch caliber absorbed completely in approximately three weeks.

It was, of course, futile to attempt to draw any conclusions until we knew definitely what commercial magnesium was and how it might be modified. The Bureau of Mines of the Department of the Interior kindly cooperated in an effort at solution of this part of the problem, and submitted the following report:

Commercial magnesium is known to contain relatively large amounts of other metals and foreign matter, including silicon, oxids, carbids (from melting under illuminating gas) and alkali chlorids. The tendency of these is to reduce the ductility of the metal, since we know, as a general principle, that a pure metal is more ductile than its alloys. In fact, it seems quite possible that pure magnesium would be much more ductile than the commercial metal. If this

5. In 1878 Dr. E. C. Huse, an American, recommended magnesium ligatures, stating that he had used them three times. His clinical report is fragmentary and furnishes no clue as to the preparation of the ligatures (Chicago M. J. & Examiner, August, 1878, p. 171).

proves true, any work on magnesium alloys should be prefaced by the production of pure magnesium, in order that the benefit of its maximum ductility may be obtained in its alloys. This question of the ductility of pure magnesium is considered so promising that a search of the literature will be made for methods of magnesium reduction and properties of the pure metal.

Besides producing the pure metal by reduction, it might be possible to refine the commercial grade by distillation in vacuo. This has been done by Marden and Rich with aluminum. They obtained beads of aluminum which were "substantially free from iron and silicon."

A rather hasty review of the literature dealing with alloys of magnesium has been made. Only those alloys have been considered, for the time being, in which a reasonably ductile metal is alloyed with magnesium. For example alloys of silicon and magnesium have not been considered since the possibility of their possessing marked ductility is extremely small. Many of the metals which might alloy with magnesium are probably toxic. It seems wise, however, to leave the question of toxicity entirely up to the medical cooperating agency, attention having been called to the fact that the chemists idea of toxicity is usually gained from the action of metal or salt when introduced into the body through the alimentary or respiratory systems. Their action when implanted in the tissues might be entirely different. Mercury and its salts when taken by mouth are highly toxic, yet it seems to be possible to use mercury compounds in large dosage, given intravenuously, without danger.

The noble metals alloy with magnesium, and may increase its ductility. The question arises as to whether they would so increase the nobility of the magnesium that it would not longer dissolve. Also as to whether the more noble metal would be left behind in the tissues, and, if so, in what form.

Furthermore, it is fairly safe to expect marked ductility only in alloys which are solid solutions of one component in another. This, of course, is not an invariable rule, but it is a safe working guide in searching the field for possibilities. Magnesium and gold form alloys which contain several series of solid solutions of the type $AuMg_2$ and Mg_2Ag. No data as to the malleability of the alloys is available.

The compounds of magnesium and cerium are brittle and have a hardness of 3 to 4.

The magnesium-calcium series contain no solid solutions.

Magnesium and potassium are immiscible, according to Smith,[6] but Thorpe[7] says that magnesium and potassium form malleable alloys which decompose water at ordinary temperatures.

Also, according to Thorpe, the alloy of magnesium with 5 per cent. thallium is more ductile than pure magnesium. It should be noted here that thallium is ordinarily considered a toxic metal, the thallous salts having chemical properties resembling those of the mercurous form of mercury. Thallic salts are not very stable and are formed only under strongly oxidizing conditions. The hydroxid of thallium is soluble and somewhat resembles the alkali hydroxids in chemical properties. The physical properties of the metal itself are said to be similar to those of lead.

Thorpe lists as being brittle, the alloys of magnesium with aluminum, cadmium, zinc, bismuth, antimony, silver, gold, platinum and the ternary alloys magnesium, lead, bismuth and magnesium, copper and gold. This data is probably not at all reliable.

---

6. Smith: Ztschr. Anorg. Chem. **56**:109.
7. Thorpe: Dictionary of Applied Chemistry, p. 370.

From this report, it was apparent that the properties of chemically pure magnesium must be studied. It was hoped that the Bureau of Mines would participate in this part of the study, but unfortunately the postwar pressure of work rendered such participation impossible.

Just after the receipt of the foregoing report, Dr. F. N. Kannenstine of the Department of Physics of the University of Chicago kindly supplied me with a very small quantity of chemically pure (distilled in vacuo) magnesium strips. With these, some preliminary experiments were made on rabbits and white mice. This chemically pure metal was found to absorb at about the same rate as the commercial metal.

Small pieces of strip were planted subcutaneously in the ears of rabbits. In every instance, the site of the implantation developed into a wheal, due to a subcutaneous exudate of serum. The same fact had been noted previously in similar experiments performed with commercial magnesium, but the exact cause of the exudate was not studied.

In a series of four white rats, the pure magnesium strip was implanted (sterile technic) in the subcutaneous tissue of the back. After two weeks, two of the rats were killed with chloroform and the site of implantation inspected. It was found that in both animals the magnesium had disintegrated, but that the residue (calcined magnesia) was imprisoned in a gas cyst, the size of a large pea. The other two rats were killed after six weeks, and showed complete absorption of the magnesium with no gas cysts present. Dr. Leo Loeb furnished the animals for these four experiments and made the implantations for me.

These experiments demonstrated definitely both the tendency to exudate formation (experiments with rabbits' ears) and the early formation of gas (hydrogen) at a rate more rapid than its absorption. Unfortunately, however, these experiments exhausted the supply of pure metal.

Mr. S. K. Colby, president of the American Magnesium corporation, Niagara Falls, N. Y., in an admirable spirit of cooperation, rendered assistance at this point, furnishing unlimited facilities, effort and expense toward the ultimate solution of the problem of the production of a ductile, strong magnesium wire. Anyone who has ever encountered the difficulties incident to medico-industrial research will appreciate what such cooperation meant. The report from the research department of the American Magnesium Corporation is appended to this paper.

The first efforts of the American Magnesium Corporation laboratory was to supply a chemically pure metal which could be extruded and drawn into wire ranging in caliber from 0.007 inch, upward. The first samples of wire were sufficiently pure to warrant the execution of animal experiments in definitely planned order. The tensile strength of this

first wire was so poor that we knew we were not dealing with a definitive product, and we therefore deliberately postponed experiments in hemolysis, bacteriolysis and gas production, until we were sure we were dealing with the final product.

I shall make no mention, in the body of this paper, of the various expedients resorted to in order to secure a suitable wire from the various points of view of strength, ductility, absorption, and gas evolution, because these topics are taken up fully in the appended metallurgic report.

OBJECTS OF BIOLOGIC STUDY

As soon as we had in hand a pure magnesium wire, but before we had developed an adequately strong and pliable suture, work was started on biologic studies. These studies were made on dogs and rabbits, under full surgical anesthesia, and with human blood serum in vitro. The objects of these studies were to determine: (1) length of residence of magnesium in the tissues; (2) fate of the magnesium; (3) evolution of gas; (4) fate of the gas; (5) microscopic effects of magnesium on the tissues; (6) microscopic effect of the tissues and body fluids on the magnesium, and (7) systemic effect of magnesium.

1. *The Absorption Time of Magnesium.*—The experiments showed that the rate varied both with the size of the implanted wire suture and the type of tissue in which it was imbedded. The ear of a rabbit is not richly supplied with blood, under ordinary circumstances. Magnesium implanted in this region, therefore, takes a longer time for absorption than does the same quantity of the metal implanted in a richly vascularized region. Sutures of 0.007 inch caliber placed in muscle absorbed within from twenty-four to forty-eight hours. Sutures of larger caliber took a proportionately longer time for absorption. When the caliber was 0.01 inch, from ten days to two weeks was necessary for absorption. Sutures of a given gage could be counted on to absorb with more regularity than is the case with catgut.

2. *Fate of the Magnesium.*—If the area of implantation was inspected early, we found small particles of metallic magnesium and a soft granular detritus that undoubtedly represented magnesium oxid, as described by Payr. If the wound inspection was made later, there was no vestige of magnesium or its salts. Absorption was complete.

3. *The Evolution of Gas.*—In our experiments, the evolution of gas presented itself as a much more serious problem than we were led to expect by the statements of Lespinasse. Our earliest experiments on rats resulted in the formation of gas cysts. These cysts, it is true, were absorbed in time, but it is equally true, and much more important, that their occurrence early in wound healing tended to create a most undesirable separation of tissues and layers. When we placed mag-

nesium in human blood serum (in test tubes) at body temperature, the evolution of gas was so rapid as to render the serum opalescent, owing to fine gas bubbles. The gas evolved responded positively to the test for hydrogen. Various means were employed to delay gas production, such as paraffin and metallic coatings (so-called bimetallic wire), but without result.

4. *Microscopic Effect on the Tissues.*—Microscopic examination of excised blocks of tissue through which magnesium wire had been passed, showed a remarkable absence of leukocytic reaction. If leukocytic infiltration is taken as a criterion of tissue reaction, it may be said that muscle, skin and subcutaneous tissue showed practically no reaction to magnesium. On the other hand, the tissues presented definite evidence of gas formation, as shown by: (*a*) separation of muscle cells and bundles; (*b*) the presence of small cysts, up to the size of 2 mm. in diameter, some of them containing serum, and (*c*) the fact that the suture itself lay in a tunnel, which seemed to be made by the pressure of gas on the surrounding muscle.

5. *Microscopic Effect of the Tissues on Magnesium.*—Removal of the sutures at various stages, and examination under the microscope, showed that the body fluids had a peculiarly irregular corrosive effect on the magnesium. The wire did not dissolve as does a stick of candy, but was eaten out irregularly, a deep defect at one point of the circumference set over against almost no absorption at its opposite point, and undulating defects here and there, with intervening sharp angular absorption defects. All of this meant that, although absorption seemed to be taking place steadily and evenly, the integrity of the suture was sadly compromised long before absorption was even well under way. This disadvantage was easily met, by the construction of wire cables. A cable of seven strands of 0.007 inch magnesium wire made a suture of about the same caliber as No. 2 catgut.

6. *Systemic Effect.*—In no instance were we able to detect any toxic effect on the animal as a result of implanting large amounts of metallic magnesium. In view of the fact that the metal is reduced to magnesium oxid, with the evolution of hydrogen, there would be no reason to expect any type of mineral poisoning.

Up to this stage of the work, we had developed the facts that, from a purely mechanical standpoint, magnesium could be so modified as to render it adaptable to surgical uses; and that, from a purely surgical standpoint, the only disadvantage encountered was the accumulation of gas to such a degree that it tended to cause gas cysts and gas filled tissue spaces. There were many reasons to hope that the evolution of gas, serious obstacle though it was, could be overcome to such a degree as to render it a negligible factor.

Before attempting to do this, however, it was decided to investigate the more specific biologic reactions of magnesium. In this portion of the experiment on the properties of pure magnesium, the work was limited to a laboratory investigation of the hemolytic, proteolytic and bacteriolytic properties of the metal. All of these tests were made with pure magnesium wire approximately 1.25 mm. in diameter. The wire had a dull gray tarnished surface when received. Immediately before each test, the wire was thoroughly scraped with a knife to expose a bright glistening surface of pure unaltered magnesium metal.

The following experiments were made to determine the hemolytic properties of the metal. Wire cut into pieces 2 cm. long, was placed in sterile Petri dishes and covered to a depth of 2 mm. with freshly prepared blood-agar. Three other dishes of blood-agar were poured and when they had solidified, pieces of wire were dropped on the surface and pressed down until on a level with the surface of the medium. Within a few hours, gas bubbles were noted on the submerged pieces of magnesium. After twenty-four hours, a faint zone of hemolysis could be seen around each piece of wire, in those lying on the surface as well as in those embedded underneath. The red opacity of the mediums became a slightly darker red, and a wine red transparent zone around the wire gradually increased for three or four days. This zone of hemolysis varied from 3 to 6 mm. beyond the wire.

In a second series of tests, 0.5 c.c. of red cells from defibrinated sheep's blood was added to 5 c.c. of an 0.85 per cent. sodium chlorid solution and centrifuged. The overlying salt solution was clear without any trace of hemolysis. In each of six tubes, 3 cm. of magnesium wire was dropped. An equal number of tubes with blood cells but without wire were used as controls. All of the tubes were placed in an icebox, and when examined twenty-four hours later, there was found, in each tube which contained wire, a zone of hemolysis, which gradually increased for three or four days. The control tubes showed no hemolysis during that time.

In the first set of tubes, it occasionally happened that the gas evolved would cause the piece of wire to float on the surface of the saline solution, in which case there was little or no hemolysis. In later experiments, with the use of a tube of small diameter and a larger wire whose weight was sufficient to keep it on the bottom, the hemolysis was constantly noted.

PROTEOLYSIS TESTS

On the surface of six coagulated blood serum slants such as are used for growing diphtheria bacilli, pieces of wire were placed. In six other tubes, the wire was pressed into the coagulated serum. All tubes were incubated for ten days. Examination failed to show any

proteolysis. In a second series of tests, twelve tubes of blood serum (serum, 3 parts; bouillon, 1 part) were carefully heated until the mixture coagulated to the consistency of soft jelly. Wire was laid on the surface of six slants. In six, the wire was pressed into the mediums. All were incubated for ten days. In these tubes, where the wire had been pressed into the serum the bubbles of gas had so torn the mediums that it was impossible to demonstrate lysis; but where the wire had been laid upon the surface of the slant, there was a distinct liquefaction of the serum. The wire was found lying in a small trough with eroded sides and bottom.

BACTERIOLYSIS TESTS

In the foregoing experiments for testing hemolysis and proteolysis, none of the tubes containing wire became contaminated, although no attempt had been made to sterilize the wire, and it had been handled without any care. Tests on pieces of wire 2 cm. in length, freshly scraped but afterward rubbed over the hands and fingers, were dropped into culture tubes of broth. After twenty-four hours at room temperature, two were found to be contaminated with bacteria, and after seventy-two hours, four more tubes were found to be contaminated. Ten days later, the remaining six were found to be sterile.

In each of six tubes containing 10 c.c. of broth, there was dropped a piece of wire 3 cm. long. These were left in the icebox for forty-eight hours, and no growth was found in any tube. At the end of seventy-two hours, one tube was inoculated with a loop of typhoid bacilli from a twenty-four hour growth on agar. The bacilli grew very slowly in this tube, but very luxuriantly in a control tube without the magnesium wire. At the end of seven days, another tube containing wire was inoculated in a similar manner. The growth in this was slower than in the seventy-two hour tube. After two weeks, it was found that the wire had appreciably dissolved in the broth, and in none of the remaining four tubes could typhoid bacilli be cultivated.

In a number of Petri dishes one or more pieces of wire were placed, and these were covered with melted agar previously inoculated with a loop of typhoid bacilli culture. In all of these, the colonies grew over and around the embedded wire. When the plates containing wire and agar were placed in the icebox for seventy-two hours and then inoculated on the surface with streaks of typhoid bacilli, the colonies did not develop within 0.5 cm. of the wire.

These experiments show conclusively that metallic magnesium has a distinct inhibiting effect on the growth of bacteria. This bacteriolytic property was not so marked as to indicate a violently destructive action. It seemed rather to be an inhibiting action. It is unfortunately true, however, that the experiments showed also that magnesium possessed

distinct hemolytic and proteolytic properties. Hemolysis and proteolysis are undoubtedly responsible for the frequent instances of accumulation of serum in wounds sutured with magnesium wire.

No adequate method could be devised whereby the evolution of hydrogen gas could be delayed or stopped. Similarly, no method could be devised to counteract the undesirable hemolytic and proteolytic effects of magnesium. So, although the metallurgic phase of the problem may be considered fairly well solved, we must admit defeat so far as overcoming the biologically undesirable properties of magnesium is concerned. The disadvantages and obstacles encountered may not be insuperable, and it therefore should not be assumed that the subject of absorbable metallic sutures is closed.

THE MANUFACTURE OF A MAGNESIUM SUTURE FROM A METALLURGIC STANDPOINT: A REPORT FROM THE RESEARCH DIVISION OF THE AMERICAN MAGNESIUM CORPORATION OF NIAGARA FALLS, N. Y.

The possibility of obtaining a metal suture and ligature material has been a matter of interest among surgeons for a number of years. Attention has lately centered on magnesium, this element having properties peculiarly fitting it for comparison with the nonmetallic suture materials now in use. It has been known for some years that magnesium wire is rapidly corroded by the fluids of the human body and that the salts formed are readily absorbed and are presumably nontoxic in their reactions. Also, magnesium metal wire can be sterilized by boiling in distilled water, with no deterioration.

In adapting the metal for this purpose, there were several requirements to be met:

1. A wire of sufficient tensile strength to withstand the strain of sewing and tying.

2. A wire of sufficient pliability or ductility to withstand the flexing encountered in tying the surgeon's double knot.

3. A wire of high and uniform purity to insure corrosion taking place uniformly when in contact with blood serum.

4. A wire permitting some measure of control in the rate of absorption.

The metallurgic investigation which resulted in a wire mechanically suitable for the purpose was begun by a study of the influence of impurities in the metal itself. These impurities were of two kinds, foreign metallic substances and nonmetallic substances. It was quickly found that all nonmetallic substances must be very carefully excluded.

Their presence in the final wire caused nonuniform tensile strength, and annoying breakages resulted. These impurities were composed largely of magnesium oxid, formed during the melting of the metal. The development of a vacuum casting process eliminated trouble in this direction. The metallic impurities consisted of such elements as silicon, iron, aluminum and calcium. It was found that the flexibility or ductility was higher when these impurities were low. The investigation resulted in the production of a magnesium wire in which the total impurities amounted to not over 0.01 per cent. With wire of this purity not only was the ductility improved, but it was also found that the corrosion of the wire in blood serum was more uniform and might even be standardized.

The manufacturing processes leading to the production of this wire consisted of purifying the magnesium by a refining operation until a magnesium content of 99.99 per cent. was reached. This extremely pure metal was melted in a specially designed vacuum furnace and cast into cylindrical billets. These billets were put into an extrusion press, where pressures and temperatures within workable limits resulted in the production of a wire with suitable physical properties and a diameter of approximately 0.03 inch. It was determined that high ductility is an essential requirement for a suitable wire. Ductility in magnesium has been found to be dependent on the size of the grain structure. If the grain size is small, the ductility is high, and vice versa. Manipulation of the metal such as would take place in its deformation in an extrusion press tended to decrease the grain size, and therefore to increase the ductility. Considerable variation in tensile strength, ductility and surface was obtained by varying the pressure and temperature of extrusion. Generally speaking, the most satisfactory product was produced by using a temperature as low as possible.

A low temperature naturally resulted in higher extrusion pressure, and the product had the high tensile strength and elongation necessary for the subsequent operation of wire-drawing. The extrusion was not possible at temperatures lower than 225 C., and it was not found practicable to produce a wire of a smaller diameter than 0.03 inch.

The necessary further reduction in diameter was made by drawing the wire through sapphire dies. This wire-drawing involved two principal variables: the temperature of the die, or of the metal as it passed through the die, and the amount of reduction in each pass. It was determined that if the wire was maintained at a temperature of about 150 C. with a 5 per cent. reduction, it was possible to draw the wire from 0.03 inch in diameter to 0.005 inch, without intermediate annealing. With these conditions, the wire was pliable and ductile, and it became more so as the drawing continued.

It was determined that, if the drawing was attempted at temperatures much above 200 C. or below 150 C., the wire became brittle, and it was then necessary to have intermediate annealings in order to secure the necessary ductility to avoid excessive breakage. In practice, it was found easier to pass wire through a heated oil bath and then through the die. In this case the die was not heated except by the heat generated in drawing. The tensile strength and elongation of the wire could be varied by changing the temperature of the oil bath and the rate of drawing. A few of the representative results obtained are presented in Table 1.

TABLE 1.—*Variations in Tensile Strength and Elongation*

Diameter of Wire Inch	Tensile Strength Per Square Inch Pounds	Elongation in 24 Inches Percentage
0.020	35,170	4.0
0.015	39,044	2.8
0.010	43,513	1.73
0.009	43,333	1.37
0.007	45,610	1.20

TABLE 2.—*Additional Tests*

Sample	Diameter Inch	Tensile Strength Per Square Inch Pounds	Elongation in 24 Inches Percentage
Medium Hard Chromic No. 2....	0.020	46,600	8.3
Plain No. 2.....	0.020	64,000	6.25

Some tests made on a standard catgut No. 2 medium hard chromic and No. 2 plain are presented in Table 2.

It must be noted in these tests that the elongation given is that percentage which the test specimen had taken as a permanent set after breakage occurred. Owing to the elasticity of catgut, the stretch before breakage was greater than this elongation indicates. For this reason, it is difficult to get a direct comparison of elongation between catgut and a metallic wire.

Knot-tying ability is a complex which it is rather hard to analyze. It might be roughly defined as the workability of the metal and is closely connected with flexibility and ductility. In the smallest sizes, such as 0.005 inch diameter, the double knots could be tied with ease; while in the larger sizes, such as 0.008 inch diameter, some difficulty was encountered owing to the larger bulk of the wire. In order to overcome this trouble and to be able to supply a satisfactory material

for all applications, a cable was developed composed of seven magnesium wires of small and equal diameter. Such a cable composed of seven wires, six laid symmetrically around a center strand, resulted in a diameter only three times the diameter of a single wire. For example, if seven wires of 0.007 inch diameter were used, the finished cable would have a maximum diameter of only 0.020 inch, which is about that of No. 1 catgut with a tensile strength equivalent to the sum of the seven wires, and a flexibility equivalent to a wire of an approximate diameter of 0.010 inch. This cable seemed to embody all of the mechanical properties required for proper handling and knotting. When seven wires of equal diameter were employed a perfect lay resulted with each of the outside wires touching its neighbor. This gave the cable an additional advantage in that there was some control of the corrosion and absorption rate. The outer strands were corroded first, while the inner strand was for a time protected, and it, therefore, retained its integrity of section for a maximum of time. These cables compared favorably in diameter with the catgut mentioned above.

Other cables, each using seven magnesium wires of 0.005 inch and 0.008 inch diameters, were made. All of them showed more than sufficient strength for the closest double knot, and seemed from a mechanical standpoint to meet all the conditions for a suture material.

When the metallurgic research work had progressed to this point, the surgical research work of Dr. Seelig developed the fact that gas cysts formed around the metal suture. It was, therefore, evident that contact with the body fluids and tissues caused the evolution of hydrogen gas at a rate too rapid to permit of absorption. Considerable investigation was made on this detail of the problem, and an alloy wire was made and tested, with the hope of reducing the rate of gas evolution. Inferior physical properties were encountered in this material, while the rate of gas evolution was unchanged. Surface coatings were tried and the possibility of a bimetallic wire was examined. The net result of these experiments seemed to indicate that, from a metallurgic standpoint, the rate of gas evolution was substantially constant, and that no satisfactory method of control was probable.

At this point in the investigation, the biologic research apparently developed the fact that magnesium metal in contact with the blood caused hemolysis. When this result was reached, the metallurgic investigation was dropped. The work had been carried far enough to result in a satisfactory process for making a wire or cable which, from a mechanical standpoint, was entirely suitable as a suture material. It is unfortunate that a metal so nearly ideal for this surgical use apparently should possess inherent medical disadvantages that preclude its use in this direction.

EXCERPTS FROM ARTICLES ON UROLOGIC SURGERY WITH COMMENTS

E. STARR JUDD, M.D., WILLIAM F. BRAASCH, M.D.
ALBERT J. SCHOLL, M.D.
AND
LINWOOD D. KEYSER, M.D.
ROCHESTER, MINN.

KIDNEY

Exposure of the Kidneys.—Richer [1] advocates what he terms the topographic kidney incision, by means of which he is able to make an opening directly over the kidney, pelvis and upper ureter.

The incision through the skin is vertical and within the border of the sacrolumbar muscular mass, 3 cm. from the spinous processes and extending from about the level of the twelfth rib, 6 or 8 cm. toward the posterior superior iliac spine. The fascia is cut and the muscle split. The aponeurosis of the transversalis muscle, which opens on a layer of connective tissue containing the roots of the ilio-inguinal and iliohypogastric nerve, is split. These should be preserved. The fatty capsule of the kidney is then seen, and when this is opened the kidney and its pedicle are disclosed.

This incision is satisfactory for nephrotomy, for the removal of small kidneys, especially those lying close to the spine, and it is ideal for nephropexy, as the wound is directly over the area of fixation. It is also suitable for pelviolithotomy and pyelo-ureteral plastics and in primary ligations of the renal pedicle preparatory to nephrectomy.

[ED. NOTE.—This incision apparently offers an excellent exposure of the renal pelvis and the vascular pedicle and would permit good dependent drainage. In some renal anomalies, it might permit a better manipulation of the diseased parts, especially the isthmus of horseshoe kidney. Incision through the lumbar muscles makes a deep set wound and opens a wide area of muscle tissue, and would require constant difficult retraction for satisfactory exposure.]

In a split muscle incision for exposure of the kidney, described by Kolischer and Katz,[2] the skin is incised halfway between the last rib and the iliac crest. Skin and fascia are then stripped back on either side, and the approach to the kidney is made through a gridiron incision

1. Richer, V.: Chirurgie rénale par la gaine sacro-lombaire, J. d'urol. **16**: 7-11, 1923.

2. Kolischer, G., and Katz, H.: Pyelotomy, Ureterolysis, and Extirpation of the Kidney; a Special Technic, J. A. M. A. **80**:1757 (June 16) 1923.

by blunt division of the external oblique and transversalis muscles in turn, until the renal fascia is reached. Small kidneys can be delivered through this wound, but if necessary the muscles can be cut as in the usual lateral incision.

A description is given of the procedures of pyelotomy; irrigation of the kidney with sterile water to remove sand and stone debris; fat transplantation over the ureter after ureterolysis follows, and the use of double fenestrated aneurysm needles in carrying ligatures around the renal pedicle.

Lower [3] considers nearly all tumors of the kidney malignant. Nephrectomy is the operation of choice, with resection of as much as possible of the perinephric tissue. This should be followed by roentgen-ray treatment. Stone is best treated by pyelotomy, the incision being extended up into the cortical substance if necessary, as advised by Eisendrath. In bilateral stone operation should always be performed if the condition of the patient warrants. Lower does not believe that the mere presence of tuberculosis bacilli in the urine is an indication for nephrectomy. If the lesions found at operation are only small, without encapsulation, resection not infrequently lights up a general miliary tuberculosis. It is better to wait until an abscess has formed and has been walled off. Lower also delays operating in cases of so-called multiple septic infarct in the early stages. Many patients recovered spontaneously. If well defined abscesses develop, nephrectomy is indicated.

Hinman's work on hydronephrosis has shown that the unilateral hydronephrotic kidney seldom recovers its function once the opposite kidney has undergone compensatory hypertrophy. This is sufficient indication for nephrectomy rather than the mere relief of obstruction in cases of long standing.

[Ed. Note.—Lower brings out several points in the handling of tuberculosis, septic infarction and unilateral hydronephrosis that are at variance with the methods usually employed. The incision and manipulation necessary to expose the kidney which harbors the bacilli of miliary tuberculosis would offer a chance of spreading infection in itself, and the perinephritic adhesions encountered at a second operation after the abscess had formed and the process had been walled off would offer greater risk of infection and spreading of the disease than primary removal of the kidney.]

Renal Anomalies.—Caulk [4] reports six cases of ectopic kidney, four being single, with the other kidney in the usual situation. The fifth case

3. Lower, W. E.: Operation of Choice in Surgery of the Kidney, Ann. Surg. **78**:250-254 (Aug.) 1923.

4. Caulk, J. R.: Surgery of the Ectopic Kidney, Ann. Surg. **78**:65-75 (July) 1923.

was a congenital fused unilateral ectopic kidney with two pelves on the right side. Suspension and fixation of the kidney to the lumbar fascia partly relieved pelvic pain, and a constant desire to micturate. The sixth case was one of complete fusion of both kidneys, the mass lying over the sacral promontory. Etiologic features associated with the embryonic development of the blood vessels and their lack of obliteration as the kidney starts to ascend to the renal fossa are brought out.

Stasis leads to hydronephrosis and renal infections of various kinds in many cases, although some persons pass an uninterrupted life so far as the kidney is concerned. Nephrectomy is indicated when there is disturbance, and sometimes in young women who may become pregnant; but only when the condition is unilateral.

[ED. NOTE.—The fixity of these kidneys, the multiple blood supply, and the short, tortuous ureter are responsible for a relatively high morbidity in cases of pelvic kidney. On the other hand, not infrequently apparently normal ectopic kidneys have been discovered during abdominal exploration, and the patients were in good health many years later.]

Stewart and Lodge[5] reviewed the renal anomalies in 6,500 necropsies. A horseshoe kidney was found in fourteen cases, unilateral fused kidney in one case, pelvic kidney in three and a congenital absence of one kidney in sixteen.

In six of the patients with absence of one kidney, death was due to disease in the solitary kidney; in three cases, to nephritis; in two cases, to infection, and in one case, to stone formation. There was no disease in the remaining ten cases. Six patients were over 55 years of age and one died in his eighty-first year, from fracture of the skull.

Two of the three patients with pelvic kidneys died of other conditions, one aged 53 years, the other, 63. In the third case, there was a solitary right pelvic kidney with a single artery from the aorta and a short, kinked ureter. The patient, aged 55, died of renal infection.

The authors collected twenty-eight cases of unilateral fused kidney. The displaced organ generally lies below the normally situated one, its upper pole fused with the lower pole of the latter. The ureter from the upper kidney generally enters the same side of the bladder. Usually, three or four arteries pass to the fused organ, of which two supply the upper and two the lower half. One or both vessels to the upper kidney arise directly from the aorta, in or below the normal position. The vessels for the lower kidney are more irregular. They may arise from the lower part of the aorta, at the level of the bifurcation, or they may spring from the common iliac of the opposite side.

---

5. Stewart, M., and Lodge, S.: Unilateral Fused Kidney and Allied Renal Malformations, Brit. J. S. **11**:27-37 (July) 1923.

[Ed. Note.—As a result of ureteral obstruction, a deficient pelvic drainage and trauma, fusion and displacement, anomalies of the kidney frequently cause disease in early life. The age of a number of the patients reported in this article, dying of other conditions, without renal disease, indicates that it is possible to live a life of normal length, even with markedly abnormal kidneys. In two patients with horseshoe kidney, one aged 70 years, and one aged 82, and in two patients aged 50 having pelvic kidney, no renal disease was found. In only one of fourteen cases of horseshoe kidney was there grossly visible renal disease. In most cases of congenital absence of one kidney, the remaining kidney is normal.

Nephrolithiasis.—Federoff [6] suggests the theory of nephrotoxins, that the mate of a diseased kidney also becomes affected from the toxins of the disease, and a deleterious action is exerted on the normal kidney, especially when the diseased kidney is infected or contains stones.

Two hundred and fifty cases of nephrolithiasis are reviewed. Of the total number of patients, twenty-eight (11.2 per cent.) died the first nine months after operation. Five died from uremia, two from anuria and five from cardiac, and nine from pulmonary conditions.

In fifty-five aseptic cases, there were no deaths. In sixty-nine pelviolithotomies and twenty-three ureterolithotomies, there were no deaths. Eight of forty-two patients who had had nephrolithotomies (18.8 per cent.), and only nine of ninety-three who had had nephrectomies (9.3 per cent.), died. Five of ten fleshy patients on whom nephrolithotomy was performed died.

The author advises that stones be removed through the renal pelvis, or if the pelvic incision is insufficient, that it be combined with a small incision in the parenchyma. The typical nephrolithotomy should only rarely be performed. Nephrectomy should be performed in most cases, in which there is extensive stone formation, especially if there is a hydronephrotic atrophy of the renal parenchyma, or if there are multiple stones imbedded in the parenchyma.

[Ed. Note.—Federoff's statistics dated from 1903, a time when the mortality for any renal operation varied from 10 to 20 per cent. Unquestionably, the cases in which operation has been performed more recently would afford even more favorable mortality data than are found in his article. Federoff's statistics compare favorably with those of Israel reported in 1918. Many of Israel's patients were also operated on at a period when renal operations carried a high mortality. Israel reports 335 nephrolithotomies with twenty-three (6.8 per cent.) deaths; 102 nephrectomies for calculous pyonephrosis with eight (7.8 per cent.)

6. Federoff, S. P.: Zur Klinik und Therapie der Nephrolithiasis, Ztschr. f. Urol. **16**:56-82, 1922.

deaths, and 127 cases of pelviolithotomies with three (2.3 per cent.) deaths.]

In the removal of large branched stones, Pappa [7] has modified the technic of nephrotomy so as to minimize the incision and the trauma to renal tissue. He exposes the kidney, inserts a finger into the renal pelvis and presses the stone toward the cortex. An incision is then made directly over and down to the stone, following all its contours, which permits the stone to be easily removed without breaking. The kidney is closed by passing a suture completely around the long axis of the kidney. This is fixed at several points to the renal capsule. Several sutures are then passed over the concave portion of the kidney, closing the line of incision, but not penetrating the kidney tissue. These are tied to the long transverse suture. The kidney incision is closed completely, and drainage is carried out through the pyelotomy incision.

[ED. NOTE.—Nephrolithotomy at the present time is only rarely performed in this country. Federoff has repeatedly advised against it. The majority of renal stones may be removed through the renal pelvis. The small amount of renal function remaining in a stone-forming kidney, especially after a wide splitting exposure, does not compensate for the risk of postoperative infection and hemorrhage.]

Eliot [8] asserts that persistent irritation after the removal of a renal calculus may be due to the abnormal urine from which the stone was precipitated. Pelviotomy for renal stone is urged in preference to nephrotomy, and the technic of bimanual palpation with one finger in the pelvic incision as a means of localizing the stone on the operating table is described.

In bilateral lithiasis, nephrorectomy is justifiable only if there is marked pyonephrosis, and only then if the other kidney has enough demonstrable function to support life.

Further chemical study of the urine, with comparison of affected and unaffected sides, is urged as a possible source of etiologic information.

[ED. NOTE.—The fact that specific bacteria will produce urinary lithiasis has been shown experimentally by Rosenow and Meisser, while Keyser has produced stones under aseptic conditions by causing an excessive excretion of urinary crystalloid. Clinical, bacteriologic and chemical studies from these two standpoints are greatly needed.]

Phemister [9] reviews calcification and ossification in the urinary tract and reports two rare and unique cases of renal calculus attached by

---

7. Pappa: Technique de la nephrotomie dans les gros calculs coralliformes, Bull. et mém. Soc. de chir de Paris, **6**:250-255, 1923.

8. Eliot, E., Jr.: Certain Features of Renal Calculus, Ann. Surg. **78**:231-239 (Aug.) 1923.

9. Phemister, D. B.: Ossification in Kidney Stones Attached to the Renal Pelvis, Ann. Surg. **78**:239-250 (Aug.) 1923.

a pedicle to the renal pelvis. In each of these cases, the central portion of the calculi showed areas of ossification with true marrow cells, fat, fibrous tissue and capillaries in the cancellous bony tissues.

[ED. NOTE.—Stone is a chemical deposit and a nonliving foreign body so far as the kidney is concerned. Phemister's hypothesis that the calculi were invaded by the fibrous pedicle, or grew around it, and that ossification came as the result of metaplasia in the tissues of this pedicle is logical.]

Hydronephrosis.—Quinby [10] reports six cases of hydronephrosis due to constriction of the ureteropelvic juncture by an anomalous renal artery. Two anatomic varieties of anomalous vessels are described: 1. The kidney may have an artery running to each pole with no vessel entering the hilum. 2. Besides the normal blood supply to the hilum, there may be a second polar artery going to the lower pole of the kidney. Such anomalous vessels may originate from the aorta independently or from the ovarian, spermatic or iliac arteries. They represent persistent arteries of the mesonephros that have failed to become obliterated after the ascent of the kidney. Dilatation of the pelvis, thinning of the renal cortex and all degrees of renal destruction have been found. The ureter is generally not dilated below the obstruction.

The disease occurs in young persons, usually starting in the second decade. Pain in periodic attacks is common, either in the costovertebral angle or high in the abdomen. It does not radiate except occasionally in acute attacks, and is not infrequently accompanied by residual soreness in the renal area. There is often a dragging in the renal area. A tumor is an indication of marked pelvic dilatation. Palpation shows renal tenderness, but morbidity is generally not elicited. Urination is seldom affected, except for frequency during an attack. The renal function in combined specimens is usually normal, but there may be lowered excretion on one side in the differential function test, depending on the degree of renal destruction. Pyelography shows the dilated pelvis above the ureteropelvic juncture, and a normal ureterogram below.

The treatment is operative, nephrectomy being employed when the renal function reveals an extensive destruction of the kidney. Ligation and section of the aberrant vessel has been reported to produce cure, but is regarded as unsafe from the standpoint of the renal blood supply, especially if the vessel is large. The ideal operation, according to the author, is a plastic one on the ureter and pelvis. The ureteropelvic juncture may be widened after the manner of a Heineke-Mickulicz pyloroplasty or by free section of the ureter, with reimplantation into

10. Quinby, W. C.: Hydronephrosis, J. Urol. **10**:45-66 (July) 1923.

the pelvis at another site avoiding the vessels. In three cases, this operation was performed, with good results. In two cases, nephrectomy was performed, and in one case relief was obtained by a plastic dilatation of the Heineke-Mickulicz type. In the latter case, the pyelogram, one year later, showed marked diminution in the size of the pelvis.

[Ed. Note.—Section of the aberrant vessel has been shown by Harrington and others to cause atrophy in the area of the kidney supplied by this branch. Furthermore, collateral circulation does not become established. Plastic operations on the ureter and pelvis are not popular with most surgeons, and are only rarely performed. The good results obtained in the foregoing cases are noteworthy, and might well stimulate further clinical study.

Nephropexy.—Kostlivy [11] reports another method of tendon transplantation for the fixation of loose or ectopic kidneys. Two long strips of fascia lata are obtained, and these bands are swung over the eleventh and twelfth ribs, forming a hammock which passes around and supports the kidney. Differing from other means of tendon support, the transplants, instead of encircling the long axis of the kidney, pass across the kidney under the renal vessels, thus giving a more definite fixation. Twenty-six patients have been operated on by this method with good results. In fifteen cases, there was a complete cure. In a number of cases, pyelograms taken on an average of two years after operation reveal the kidney in good position.

Frangenheim [12] describes an anterior extraperitoneal method of exposing and fixing loose kidneys. This approach was suggested by the work of Albarran and Czerny, who were the first to remove kidneys through the anterior abdominal wall without opening the peritoneum. The incision extends from the costal margin to about 4 cm. above the anterior superior spine. If the tumor is large, the opening is amplified by extending the incision at angles toward the middle line, the upper limb running parallel to the costal margin and the lower parallel to Poupart's ligament. The muscles are divided and the peritoneum is drawn medianwards. After the kidney is freed and the fat capsule on the posterior surface is broken up, the kidney is brought to a normal location, stitched to the lumbar muscles and fixed to the twelfth rib. The peritoneal fold is then tucked up under the kidney and fixed to the posterior muscles, affording a supporting shelf for the kidney.

[Ed. Note.—Foreign medical literature and recent texts still contain many articles dealing with bizarre and complicated methods of

11. Kostlivy, S.: Eine einfache Methode zur operativen Befestigung der Wanderniere, Zentralbl. f. Chir. **50**:217-218 (Feb. 10) 1923.

12. Frangenheim, P.: Nephropexie vom vorderen Nierenschnitte aus, Ztschr. f. urol. Chir. **13**:31-34 (May) 1923.

fixation of ptosed kidneys. In the large clinics in this country, palliative operations of this type are generally no longer employed, attention in most cases being directed to an underlying pathologic condition.]

Polycystic Kidneys.—Payr [13] reports a modification of the Rovsing cystic puncture operation, which controls the disease for a period and avoids nephrectomy. The kidney is delivered in the usual way and, instead of a knife incision of only the larger cysts, all cysts visible, even the minute globules, are carefully touched with the cautery. After destruction of the outer cysts, many internal cysts may be identified through the destroyed cavities. The larger cysts are widely incised. After this operation, the kidney shrinks markedly in size. The author sutures it to the surrounding structures.

This operation, which is carried out only in case of necessity, may be repeated a number of times if occasion demands.

Tumors.—Stevens [14] has collected and draws conclusions from a group of 348 cases of renal tumor: 215 hypernephromas, eighty-six carcinomas and forty-seven tumors of the renal pelvis.

The main diagnostic points of hypernephroma are hematuria, pain, palpable tumor (85 per cent.), deformity of the renal pelvis (84 per cent.), varicocele and dilatation of the veins of the bladder, with long intervals between the attacks of bleeding.

Carcinomas make up only about 2 per cent. of renal tumors. A palpable mass is found in only 18 per cent. of the cases of carcinoma. Deformity of the pelvis was reported in every case in which pyelography was performed. Hematuria is less pronounced than in hypernephroma and papillary epithelioma. Carcinoma usually appears in patients more than 40 years of age. Calculi, which are uncommon in hypernephroma cases, are associated with 60 per cent. of carcinomas.

Papillary epithelioma of the renal pelvis is nearly always associated with intermittent hematuria (97 per cent.). Pain, palpable tumor and deformity of the pelvis and association with calculi are diagnostic features. Pelvic tumors are rarely seen in patients under 40 years of age. Metastases or transplants to the bladder and ureter are common. Complete nephro-ureterectomy is advised in cases of papillary tumors.

Corsdress [15] collected fifty-eight cases of leukoplakia of the urinary tract and added one of his own. In thirty-six cases, the leukoplakia

---

13. Payr, E.: Die operative Behandling—Ignipunktur mancher Fälle polycystischer Nierendegeneration. Bemerkungen zur Pathologie und Klinik, Ztschr. f. urol. Chir. **12**:254-268 (March) 1923.

14. Stevens, W. E.: The Diagnosis and Surgical Treatment of Malignant Tumors of the Kidney, J. Urol. **10**:121-125 (Aug.) 1923.

15. Corsdress, A.: Ein Fall von Leukoplakie des Nierenbeckens mit Bildung eines Epithelpfropfes (sog. Cholesteatom), Ztschr. f. urol. Chir. **13**:1-30 (May) 1923.

was in the bladder and in twenty-three in the renal pelvis. The disease of the bladder occurs in middle life, and is more common in men than in women. In most cases, it is chronic, existing for from one to ten years. In twenty-three of the thirty-six bladder cases, there was also acute cystitis. Eleven cases were associated with stone. Stones were present in eight of the twenty-three pelvic cases.

Retention and infection are etiologic factors in both the renal and the vesical cases. Tuberculosis is not uncommonly found. Cases are reported by Halle, Beseleir and Kretschmer.

In fourteen of the renal cases, pyelonephritis was present. Inflammation is the most common cause of leukoplakia in the pelvis. It may be either acute or chronic, and may be associated with a new growth forming in the mucosa or a mechanical inflammation from stone or extreme distension.

This condition rarely heals of itself. The renal cases require nephrectomy, and the author advises cauterization or resection of the areas in the bladder. In mild cases, bladder lavage, especially with resorcin or salicylic solutions, may be of help.

[ED. NOTE.—Leukoplakia not infrequently develops after long periods of infection and stone formation, in some cases after symptoms have been present from twenty to thirty years. It is possibly a protective response to repeated chemical or long continued mechanical irritation. It has been found in all parts of the urinary tract, and not infrequently undergoes malignant degeneration, forming squamous-cell tumors. In contrast to the chronic benign growth, these tumors are extremely malignant, spread rapidly and extensively and offer a very poor prognosis.]

Infections.—In a review of 40,621 necropsies from the Eppendorfer *Klinik*, Kümmell [16] found 119 cases of tuberculosis of the kidney. In eighty-four of the 119 cases, the condition was bilateral; in thirty-five, unilateral. In contrast to this, bilateral infection was found in only five of 100 surgical cases of renal tuberculosis. The cases which came to necropsy gave evidence of other foci of tuberculosis in 99.2 per cent., and the surgical cases, in 44 per cent.

The kidney is generally infected from the blood stream, and infection is almost always secondary to some other focus in the body. The second kidney may be infected in various ways, the infection ascending from the bladder through the ureter or lymphatics, by the blood stream or directly from the opposite kidney by means of the lymphatic connections, as described by Cathelin and Albarran.

16. Kümmell, H.: Ueber Nierentuberkulose, Ztschr. f. Urol., 1923, supplement, pp. 18-28.

It is doubtful that any patient recovers spontaneously. In 316 with renal tuberculosis who were not operated on, ninety-nine (33.3 per cent.) lived less than two years, and more than half (58 per cent.) lived less than five years. Twenty per cent. lived more than five, and 6 per cent. more than ten years.

Mortality following operation in the early cases was very high. Von Schmieden, in 1900, in a large series of cases, reported a mortality of from 25 to 35 per cent. Recent statistics give a much better outlook. Frank reported a mortality of 9.3 per cent.; Boeckel, of 5.8 per cent., and Legueu, of 5.9 per cent. Israel, in 1911, in a collected review of 1,023 nephrectomies, found an operative mortality of 12.9 per cent. and a late mortality of 14.1 per cent.

In fourteen (7 per cent.) of 188 cases of nephrectomy reported by Kummell, the patients died. During the last fifteen years, with improvement in diagnosis and operative technic, there have been no deaths. In the 174 cases, sixteen (9.2 per cent.) patients died in the first six months, mostly of miliary tuberculosis or meningitis; and in the 158, fourteen (8.8 per cent.) patients died during the next four years and four more during the second four years. After that time, there was practically no mortality from tuberculosis. Seventy-seven patients are alive and well from ten to thirty-three years after operation. Tuberculosis is primarily a unilateral disease which, after a certain time, will infect the second kidney. With an early nephrectomy, an excellent result may be obtained, with practically no deaths. From 85 to 90 per cent. of patients operated on early will be completely cured.

Kleinschmidt [17] discusses five cases of actinomycosis of the kidney reported in the literature and adds a case of his own. The patient, a man, aged 24, complained of pain in the left loin of ten weeks' duration. A fistulous tract led from the kidney to its capsule, in which the mycotic granules were found. Nephrectomy was performed, and eight years later the patient is well.

URETER

Bouniot and Rochet [18] report a case in which, during the course of an operation, the right ureter was cut and immediately sutured. An end-to-end suture was used, similar to that employed by Carrel in the suture of blood vessels. After the operation, there was a gradual onset of symptoms of renal infection, pain, temperature and pyuria. Forty-three days after operation, a pyelogram revealed beginning hydronephrosis. Eight months later, there was severe renal colic and cystitis.

17. Kleinschmidt, P.: Zur Kasuistik der primären Nierenaktinomykose, Arch. f. klin. Chir. **120**:658-661, 1922.

18. Bouniot and Rochet, P.: Suture immédiate d'une section de l'uretère; resulats éloignés, J. d'urol. **16**:42-47, 1923.

A second operation revealed an enormous hydronephrosis and hydroureter. The ureter was 1 cm. in diameter, thin walled, and adherent to the surrounding structures. The area of suture of the ureter was a solid mass of scar tissue. The ureter was straightened, and the kidney fixed to the twelfth rib. The symptoms and signs of ureteral obstruction and infection gradually subsided. Nine months after the second operation, nothing abnormal was found at cystoscopic examination, and the patient had no further discomfort. Six months, eleven months and eighteen months after the suture of the ureter, the elimination of urea and indigocarmin was normal.

Ureteral Tumors.—A review of the literature of primary carcinoma of the ureter by Meeker and McCarthy [19] reveals thirty-three cases, including one of their own. A number of these cases were found in protocols of necropsies. Few were diagnosed during life, and successful surgical removal was extremely rare. Histogenetically, these tumors arise from the epithelium of the ureter. Fourteen of the patients were females, and nineteen were males. The youngest was 15 years, the oldest 89. Fourteen patients died before operation, and eleven after operation. Pain, hematuria, palpable tumor, hydronephrosis, ureteral obstruction and induction of bleeding after catheterization are mentioned as important symptoms. Diagnosis by ureterogram was recorded once, by Quinby. The pain is relatively atypical, seldom radiating as in cases of calculus. Calculus was associated in six instances, and pus was noted in four. If a correct diagnosis is made, nephroureterectomy, when possible, is the procedure of choice. The use of the pyelo-ureterogram and search for atypical epithelial cells, especially after catheterization of the ureter, is urged as a diagnostic effort in suspected cases.

Ureteral Stone.—Crowell [20] reports 140 cases of ureteral stone removed by means of cystoscopic manipulation, and seven cases of failure. The bladder is anesthetized with from 1 to 2 ounces (30 to 60 c.c.) of a 2 to 5 per cent. procain solution, injected and allowed to remain from ten to fifteen minutes before filling with boric acid solution. The ureteral catheter is inserted until it meets resistance. Then a 2 to 5 per cent. procain solution is injected into the ureteral catheter and allowed to remain for ten minutes. Dilatation with catheter or metal ureteral sound is then carried out, oil being injected to help manipulation. If the catheter passes the stone, drainage to the kidney is established. The catheter may be left in situ, or other catheters may

19. Meeker, Louise H., and McCarthy, J. F.: Primary carcinoma of the ureter, J. A. M. A. **81**:104-109 (July 14) 1923.

20. Crowell, A. J.: Removal of Ureteral Stone by Cystoscopic Manipulation: Disintegration of Cystin Stone by Pelvic Lavage and Internal Medication, Surg., Gynec. & Obst. **37**:113 (July) 1923.

be inserted. Usually, a No. 9 French catheter will pass after a No. 6 has been in place for twenty-four hours. A case is reported of cystin calculus in the kidney. Lavage with mercurochrome-220 soluble; a low protein diet, and urinary alkalinization resulted in disintegration of the calculus.

[ED. NOTE.—An attempt at cystoscopic manipulation and removal is unquestionably indicated in most small stones situated in the lower ureter. Crowell apparently applies this procedure to most of his cases. Other investigators are more conservative, preferring surgery if the stone is more than 2 cm. in diameter; if there is acute renal infection, and if the patient is intolerant to repeated cystoscopy. The use of papaverin and other agents as relaxors of ureteral musculature has met with only doubtful success. Disintegration of calculus by chemical means has been long sought. Everything from so-called lithia water to turpentine has been tried. Crowell approached the removal of this cystin stone on scientific grounds. His results warrant the hope that other forms of calculus may some day be removed by analogous methods.]

BLADDER

Tumors.—Federoff [21] reports a series of 165 cases of tumor of the bladder. Twenty per cent. of the patients were without recurrence from two and one-half to thirteen years after operation. Thirty per cent. had recurrence during the first two years after operation. A two-stage method of total extirpation of the bladder is advocated in certain cases. The mortality in single stage extirpation of the entire bladder is extremely high. In 321 collected cases, the mortality varied from 50 to 60 per cent. Bystrow's cases of two-stage removal of the bladder, in one of which Federoff operated, are discussed. Bystrow reported eleven cases in which there was no operative mortality. Federoff adds four cases to Bystrow's series. In the two-stage procedure, the ureters are transplanted to the sigmoid flexure, both at one operation. In a few cases, the ureters have been transplanted to the loin or to the vagina. The second operation, which is performed from one to three months later, consists in removing the bladder, in most cases extraperitoneally, although a number of transperitoneal operations have been performed. Pyelonephritis is the most common complication following transplantation of the ureters, developing very readily in adults, from twenty-four to forty-eight hours after operation in some instances. Not infrequently, there is recurrence of the growth in the region of the neck of the bladder; and on this account, the urethra is removed completely in women. In the five cases in which Federoff

21. Federoff, S. P.: Ueber die totale Extirpation der Harnblase bei Blasentumoren, Ztschr. f. Urol. **17**:290-306, 1923.

operated, one patient died of pneumonia, and one of pyelonephritis shortly after operation; one lived sixteen months; one died from recurrence in five years, and the fifth was well two and one-half years after operation.

[ED. NOTE.—Extensive operations of this type have been performed only in patients who were poor operative risks, some having had multiple operations, and all with the condition so far advanced that they were but little benefited by the usual types of resection. Federoff says that more favorable results would be obtained if the operation was performed in the earlier stages. While Bystrow's statistics directly following operation are satisfactory, the late results are not discussed. In many of these cases, infection or ureteral obstruction and uremia develops, which permits recovery from the operation, but causes death in the course of several months. Only one of Federoff's five patients lived more than two years. On the other hand, patients with extensive papillary malignancy of the bladder, obviously not resectable, have been carried along a number of years on palliative cauterization together with roentgen-ray and radium treatment.]

Deaver and Mackinney [22] report their experience with 121 cases of tumor of the bladder. Eighty-one per cent. of the patients were males, usually in the fourth, fifth or sixth decades, and 12.2 per cent. had a family history of cancer. Syphilis, diabetic ulceration and tuberculoma of the bladder are sometimes confused with malignancy. A multiplicity of growths associated with cystitis is emphasized as being suggestive of malignancy. Various methods of treatment were employed, suprapubic cystostomy, cauterization, excision of the mucous membrane containing the growth, resection and fulguration. Radium alone was used in only one case. The authors hold that practically all tumors of the bladder are malignant. Papillary cancer is ten times more common than the infiltrating squamous type. Only two thirds of the tumors are amenable to treatment.

Fulguration is advised for small or medium sized single papillomas, or pedunculated carcinomas unaccompanied by cystitis. Surgery is recommended for other types. When resection cannot be performed without transplantation of the ureters, the growth may be destroyed with the cautery or high frequency current. Resection with ureteral transplantation is generally not justifiable.

[ED. NOTE.—The degree of malignancy, which depends on the rate of growth and degree of differentiation, has led to a grading of the degree of malignancy in such epitheliomas, to afford a practical index of malignancy. The belief that all tumors of the bladder are malignant is in accord with this grading. It seems that the reluctance to resect

22. Deaver, J. B., and Mackinney, W. H.: Carcinoma of the Bladder, Ann. Surg. **78**:254-259 (Aug.) 1923.

tumors involving the ureteral area is not justifiable, in the light of at least a small number of unusual results reported by various writers.]

Squier [23] groups the areas of location of tumors of the bladder into a number of definite segments, which correspond to the units of lymphatic drainage. In removing malignant tumors of the bladder, a segmental resection is carried out. When the tumor is on the anterior surface, the bladder is bisected laterally and excised down to the internal sphincter. In tumors involving the lateral walls, the bisection is made from before backward in the median line, and the line of excision of the bladder is made just above the ureteral orifice. In case the growth involves the ureteral segments, the bisection is the same, but the line of excision is just back of the internal sphincter with transplantation of the ureter. Tumors occurring at the fundus near the insertion of the urachus should be removed with the urachus and attached adventitious tissues *en masse* up to the navel. Tumors occurring in the part of the fundus that is covered by peritoneum should be removed with the attached peritoneum. In cases in which the tumor is localized to one side of the bladder, the opposite side is disturbed as little as possible, the area of postoperative absorption being thus minimized. Twenty-seven of seventy-five patients having segmental resections died following operation; twenty had recurrence or extension of the growth, and twenty-eight are alive and without recurrence from two to eight years after operation.

Bugbee [24] points out that resection of tumors of the bladder, as advocated by Gardner in a collected study of 1,702 cases, leads almost uniformly to fatal results if operation alone is relied on. Radium treatment is still highly experimental. If a tumor of the bladder does not respond readily to fulguration, it is probably malignant, and the bladder should be opened without delay. Radium applied directly to the growth by means of the insertion of needles through a cystotomy opening, endovesical applications by the urethra, and radiation by rectum have been employed. Nineteen cases are reported. The author believes that radiotherapy combined with operation has been decidedly more satisfactory than operation alone or in combination with fulguration.

Burnam and Walker [25] report a case in which an area of infiltrating cancerous ulceration of the bladder was excised. Recurrence was noted nine months later, and radium was applied in massive doses transabdominally, and in small doses intravesically. The patient is well after seven years.

---

23. Squier, J. B.: Segmental Resection of the Bladder for Neoplasm, Surg., Gynec. & Obst. **37**:179-185 (Aug.) 1923.

24. Bugbee, H. G.: Report of Cases of Malignant Growths of the Bladder Treated by Resection and Radium, J. Urol. **10**:159-171 (Aug.) 1923.

25. Burnam, C. F., and Walker, G.: Cancer of the Urinary Bladder Cured by Radium, J. A. M. A. **80**:1669-1670 (June 9) 1923.

Pedersen [26] reports a case of bilharziasis of the bladder. The patient was a boy, aged 17 years, who was born in Africa and had lived there until the age of 10, when he was brought to America. He had suffered for seven years with intermittent hematuria, not associated with pain or other symptoms. Small hemorrhagic areal vesicular blotches were found in the bladder. A careful examination was made for syphilis, tuberculosis and parasitic disease, and the ova of *Schistosoma hematobium* were found in the urine. Treatment with intravenous injections of tartar emetic were effectual in producing a cure within a few months.

In another case, reported by McCarthy and Stern, the disease had been contracted in Africa. This patient had carcinoma of the bladder. In Africa, bilharziasis seems to be related to this condition, and to phosphatic vesical calculus; for the first two diseases are more common than in any other country, and stone in the bladder is very prevalent. Eighty per cent. of the bilharziasis cases are associated with stone. The parasite gains entry to the portal vein and works against the current until it lays its eggs in narrow venules in the submucosa of the bladder. Just how these eggs escape from the venules of the submucosa to form the lesions of the bladder is not known.

[ED. NOTE.—Apparently, the association of malignant tumors and bilharziasis of the bladder is not an uncommon finding in certain countries. Goebel [27] reports a series of cases of tumors arising in association with bilharziasis, 50 per cent. of which were malignant. Squamous cell growths, a type of growth not uncommonly found associated with a long standing infection or irritation, formed the greater proportion of these tumors.]

Exstrophy.—Lotsch [28] reports five cases of exstrophy of the bladder from Hildebrand's clinic. In four cases, the Maydl type of operation was performed, three intraperitoneal and one extraperitoneal. One case was complicated by a urinary fistula and the three other patients had fecal fistulas. Three of the fistulas were closed by secondary operations. In the fourth case, a villous hyperplasia of the mucosa of the bladder in the transplanted section caused urinary obstruction, which was followed by an ascending pyelonephritis, perinephritic infection and death from peritonitis. The fifth patient was operated on by the Tuffier-Peters method of extraperitoneal ureteral transplantation, by which the

26. Pedersen, J.: Report of a Case of Schistosoma hematobium, J. Urol. **10**: 175-180 (Aug.) 1923.

27. Goebel, C.: Ueber die bei Bilharziakrakrankheit vorkommenden Blastentumoren mit besonderer Berücksichtigung des Carcinoms, Ztschr. f. Krebsforsch. **3**:369-513, 1905.

28. Lotsch, F.: Ueber die operative Behandlung der Blasenektopie, Ztschr. f. Urol. **17**:385-396, 1923.

ureters are pulled down to the rectum extraperitoneally with a rosette of bladder tissue attached, and transplanted to the bowel below the fold of peritoneum. The ureteral end necrosed, and the patient died of peritonitis. Two of the three patients died of diffuse peritonitis; one, fourteen days, the other, four and one half months, after operation. The third died of uremia two years after operation. One of the two patients living is a boy, aged 14 years, with a urinary fistula, two and one-half years after a Maydl operation, attempt to repair the fistula having been unsuccessful. The other, a man, aged 20, is apparently perfectly well eighteen months after a Maydl operation.

[Ed. Note.—These data do not indicate the present satisfactory results obtained in operations for the repair of exstrophied bladders. The recent reports of Oppel, Muguiéry and Nove-Josserand from abroad, and of C. H. Mayo and Lower in this country permit a much more optimistic outlook.]

Diverticulum.—Duvergey [29] collected three cases of diverticulum and tuberculosis of the bladder, and added one case of his own with necropsy reports and a complete histologic study. Diverticulum is usually secondary to the tuberculosis of the bladder, but in two cases the infection came directly from the kidney. The infection is generally widespread, contraindicating extensive surgical procedures.

Treatment consists in lavage and instillations into the diverticulum. Drainage of the diverticulum is indicated in cases of severe infection with retention. The drainage may be direct, into the diverticulum, or indirect, transvesically when the diverticulum is not accessible.

[Ed. Note.—Tuberculosis of the bladder, in the majority of cases, is secondary to renal infection and generally clears up after removal of the affected kidney. Extensive tuberculous infections often cause contraction and biloculation of the bladder, which may simulate but does not represent a true vesical diverticulum.]

PROSTATE

Wossidlo [30] reports a series of prostatectomies that are of interest in that they show the types of operation carried out for prostatic hypertrophy in European urologic centers. In eighty-nine of 104 cases, the prostate was removed suprapubically; in twelve, through the perineum, and in three, by the parasacral method of Voelcker. In six cases, prostatectomy was performed for atrophic prostatitis, and in ten cases, for carcinoma. Seven of the ten carcinomatous prostates were removed by the suprapubic route, one through the perineum and two through the parasacral incision.

---

29. Duvergey: La tuberculose des diverticule vésicaux, J. d'urol. **16**:1-6, 1923.

30. Wossidlo, E.: Operationsmethoden der Prostatahypertrophie, Ztschr. f. Urol. **17**:415-422, 1923.

In the eighty-nine suprapubic operations, five (5.6 per cent.) patients died. In the last seventy-eight, there were only two deaths. Twenty-eight two-stage operations were performed, with no deaths. In the first stage, besides opening the bladder, Wossidlo attaches it to the skin with a wide margin. He gives, as the indications for the two-stage operation: (1) high blood pressure; (2) disturbance of renal function; (3) infection of the renal pelves, and (4) infection of the prostate and urethra.

In the twelve perineal operations, two (16.6 per cent.) patients died, and three had incontinence. There were no cases of incontinence following the suprapubic operations.

In three of the parasacral or Voelcker type of operation, one patient died.

[ED. NOTE.—Recent foreign literature contains a number of articles on Voelcker's type of parasacral prostatectomy. Apparently, it is practiced quite frequently in German urologic clinics. It is described by Voelcker,[31] and more fully described and well illustrated by Fischer and Orth.[32]]

In this operation, the patient is placed on his abdomen in an exaggerated Kraske position, with the buttocks elevated. Under sacral anesthesia, a straight incision is made through the ischiorectal area. Pulling the rectum toward the middle line exposes the prostate. A complete removal of the prostate with a transverse section of the urethra is carried out. The urethra is then sutured to the bladder outlet. Voelcker reports fifty-four cases with two (3.7 per cent.) deaths. In two cases only was the rectum injured. There were no late fistulas and no cases of persistent incontinence. Wossidlo reports a series of seventy-five parasacral prostatectomies with an operative mortality of 2.6 per cent.

Rubritus[33] reports a series of seventy-seven prostatectomies; fifty-two one-stage, and twenty-five two-stage operations. Seven of the fifty-two patients on whom one-stage operations were performed died after operation, one from the effects of local anesthesia, two from uremia, one from a local infection and two from pneumonia. Three of the twenty-five patients on whom two-stage operations were performed died, one from myocarditis, one from perivesical infection and one from peritonitis. In the last case, the peritoneum was torn during the second-stage exposure of the bladder.

In five cases, the prostate was removed by Voelcker's method. Rubritus states that this operation is technically more difficult than a

31. Voelcker: Ztschr. f. Urol. **4**:253-330, 1919.

32. Fischer and Orth: Ztschr. f. Urol. **5**:232-317, 1920.

33. Rubritus, E.: Die chirurgische Behandlung der Prostatahypertrophie, Ztschr. f. urol. Chir. **13**:35-46 (May) 1923.

suprapubic prostatectomy, but it permits a visualized operation and perfect hemostasis. In two cases, this operation was performed as the second stage in a two-stage operation.

Tuberculosis.—Barney [34] reports a case of primary tuberculosis of the prostate. This is a much disputed disease entity. Tuberculosis in this area is usually associated with tuberculosis of the epididymis. Barney agrees with Koll that a lack of histologic examinations of hypertrophied prostates is one reason why such cases are scarce. In Barney's case, the tuberculous prostate was excised for hypertrophy. Besides the areas of hypertrophy, miliary and conglomerate tubercles were present.

[ED. NOTE.—Only one case of primary tuberculosis was found in the histologic reexamination of 1,400 adenomatous prostates (Scholl). Grossly, tuberculosis of the prostate, either primary or secondary, often resembles the large type of highly cellular prostatic carcinomas.]

Perineal Approach.—Young [35] again emphasizes the advantages of the perineal approach to the prostate and bladder in cases of hypertrophy, carcinoma, tuberculosis, calculus and chronic infections. Failure to understand the anatomy and physiology of the region is responsible for the difficulties of operators who attempt this approach. Incontinence of urine, the chief argument against perineal prostatectomy, can be avoided by opening the prostatic space back of the triangular ligament and external sphincter. The operative technic is briefly reviewed. The advantages emphasized for perineal prostatectomy in hypertrophy of the prostate are avoidance of blind surgery, conservative preservation of the ejaculatory ducts and internal sphincter, control of hemorrhage, dependent drainage, shorter convalescence and lessened danger of infection and abdominal complications. Of 1,049 patients thus treated, 3.4 per cent. died. There were no deaths in the last 198 cases.

In early cases of cancer of the prostate, the perineal approach is the most satisfactory. Young holds that from 20 to 25 per cent. of enlarged prostates are malignant. Block removal of the prostate, capsule, urethra, neck of the bladder, seminal vesicles with the overlying two thirds of the trigon and the ampullae of the vasa deferentia is advocated. The defect is repaired by anastomosing the open bladder with the stump of the membranous urethra. Of twenty patients with enlarged prostate operated on by this method, ten apparently are permanently cured. In cases of advanced cancer of the prostate, the perineal route is favorable for the direct application of radium.

---

34. Barney, J. D.: Tuberculosis of the Adenomatous Prostate, J. Urol. **10**: 81-84 (July) 1923.

35. Young, H. H.: Importance of the Perineal Route in Diseases of the Prostate and Seminal Vesicles, Surg., Gynec. & Obst. **37**:415-416 (Sept.) 1923.

Tuberculosis of the prostate and seminal vesicles is incompletely treated by simple castration or epididymectomy. A combined perineal removal of the lateral prostatic lobes, the seminal vesicles and deeper parts of the vasa deferentia, together with removal of the tuberculous epididymis or testis and the remainder of the vasa deferentia through the groin, is recommended. Likewise, chronic infections of the seminal vesicles and prostate, which lead to septicemia, arthritis and endocarditis, can best be treated by perineal excision of the vesicles, or even the radical operation, as used in tuberculosis.

Blood Pressure.—O'Conor [36] reports seventy-four cases of urinary retention due to obstruction at the neck of the bladder. Complete drainage of the bladder led to an appreciable fall in the systolic and diastolic pressures in twenty-four hours, the degree depending on the renal function and the amount of residual urine. Gradual withdrawal of residual urine from bladders was followed by a gradual fall in the blood pressure over a period of a week; whereas sudden complete emptying was accompanied by a fall of blood pressure to its lowest point in twenty-four hours in 75 per cent. of cases. On continued drainage, there was an increase in renal function and a fixed level of blood pressure was established, which is usually lower than that noted at the beginning. The postoperative drop in blood pressure is negligible if a preliminary drainage is carried out with the establishment of a fixed blood pressure level. O'Conor recommends the intravenous injection of 1,000 c.c. of 4 per cent. glucose solution before the drainage of residual urine from the bladder.

URETHRA

Tumor.—Davis [37] reports the case of a patient, aged 50 years, who had had urinary difficulty for more than four years, with profuse hemorrhage into the bladder. Suprapubic cystostomy was necessary twice in one year, for the removal of blood clots. Both urethroscopy and cystostomy were negative until suspicion of urethral tumor was aroused. A later urethroscopy revealed a papillomatous tumor of the posterior urethra, attached to a long pedicle. Fulguration of this tumor resulted in relief of urinary obstruction and of bleeding. Five somewhat similar cases are cited from the literature. Hemorrhage into the bladder with negative cystoscopic findings should lead to more careful urethroscopy.

---

36. O'Conor, V. J.: Further Observations on the Blood Pressure in Cases of Urinary Obstruction, J. Urol. **10**:135-140 (Aug.) 1923.

37. Davis, E.: Papilloma of the Posterior Urethra—the Cause of Profuse Hemorrhage and Urinary Retention, Surg., Gynec. & Obst. **37**:194-197 (Aug.) 1923.

Diverticulum.—Howze and Hennessey [38] report a case of posterior urethral diverticulum in a negro, aged 31 years, associated with stone in the diverticulum and also stone in the bladder. These calculi were removed by suprapubic cystostomy, with dilatation of the posterior urethra, and great relief was experienced, although urethroscopy, three months later, showed that the diverticulum was still present, with a moderate amount of infection. The factors leading to congenital and acquired diverticula of the posterior urethra are briefly discussed.

Calculus.—Nelken [39] reports a case of calculus impacted in the posterior urethra, with septicemia following instrumentation and removal. The septicemia persisted, and death occurred twelve days after operation. The blood culture showed *Staphylococcus albus* and *Staphylococcus aureus.* Septicemia of a transient type following urethral instrumentation is common, but death from such invasion of the blood stream is rare.

Epispadias.—Lower [40] reports a case of true epispadias in a woman, aged 30, who had had incontinence since birth. The pubic bones were separated, but the abdominal and bladder walls were intact. The Coffey operation of transplantation of the ureters into the colon was carried out with success.

Only forty-three cases of epispadias in women are found in the literature. Any type of defect in the dorsal wall of the urethra, provided the bladder walls were intact, was classified as epispadias. Lower believes that plastic operations for incontinence are of little value. He recommends ureteral transplantation in separate operations as the procedure of choice. A detailed discussion of the embryogenetic relationships of epispadias and of bladder exstrophy is given.

Stricture.—Caples [41] presents objections to employment of the sound of Gouley and the screw-tipped filiform instruments of Phillips and Le Forte, on the ground that the instruments are too large for the initial entrance to many strictures, and that the filiform frequently buckles and easily gets out of order. The author has devised a series of sounds uniform in caliber, ranging from No. 5 F to No. 13 F. These sounds are tunneled so as to slip easily over a small filiform previously passed through the stricture. The tunnel tube extends through the handle of the instrument to an attachment for a Luer syringe, thus facili-

38. Howze, C. P., and Hennessey, R. A.: Urethral Diverticula, Surg., Gynec. & Obst. **37**:392-394 (Sept.) 1923.

39. Nelken, A.: Septicemia Following Passage of Calculus Through the Urethra, J. A. M. A. **80**:1846-1847 (June 23) 1923.

40. Lower, W. E.: Epispadias in Women, J. Urol. **10**:149-157 (Aug.) 1923.

41. Caples, B. H.: Tunnelled Sounds and a Modification of the Maissonneuve Urethrotome, J. Urol. **10**:93-97 (July) 1923.

tating irrigation. Procain is applied directly to the stricture. A modification of the Maisonneuve urethrotome embodying the same principle is described.

TESTICLE AND EPIDIDYMIS

Torsion.—McKay [42] adds two cases of torsion of the spermatic cord to the 124 cases in the literature reviewed by O'Conor in 1919. Confusion of the condition with strangulated inguinal hernia, epididymitis and architis is usual, and it is generally undiagnosed before operation. Etiologic factors are abnormal attachment of the vas; the presence of an abnormally spacious sac formed by the tunica vaginalis in which the testis is suspended, permitting a movable or floating testis, or, finally, a sudden contraction of the cremaster muscle. Pain, nausea and vomiting; swelling of the scrotal contents with marked edema extending to the opposite side of the scrotal partition, shortening of the cord, with the appearance of the scrotal contents being pulled up into the groin, are chief diagnostic features. Treatment consists in detorsion, when possible, orchidopexy with evagination of the tunica vaginalis or castration when conditions of gangrene necrosis or permanent circulatory obstruction are present.

Tumors.—Eisenstaedt [43] reports a patient, aged 65 years, who had a swelling in the left testis following an operation for hernia two years before. A tumor the size of a "goose egg" was found. Microscopically, this showed areas of hyaline tissue with smaller areas of cellular, smooth muscle interspersed. The tumor arose from the epididymis. The testis was found to be normal.

A patient, aged 22 years, had had oil injected into the right side of the scrotum three years previously, through error. Progressive swelling with pain and a firm mass in the scrotum, unattached to the testes, developed. Operation was performed. A foreign-body tumor with large vesicular spaces surrounded by hyaline tissue and areas containing multinucleated foreign body giant cells was found on microscopic examination. The diagnosis of paraffinoma from unabsorbed oil was made.

[ED. NOTE.—The vesicular space, multinucleated giant cells and an extensive round cell infiltration, in many cases simulating tuberculosis, are histologically typical of paraffinoma. Often, the similarity of the condition to tuberculosis causes confusion. The diagnosis is indicated, as in the foregoing case, by the previous history of paraffin or oil injections.]

---

42. McKay, H. W.: Torsion of the Spermatic Cord with Gangrene of the Testicle. Report of Two Cases, Surg., Gynec. & Obst. **37**:373-375 (Sept.) 1923.

43. Eisenstaedt, J. S.: Fibromyoma of the Epididymis; Paraffinoma of the Peritesticular Tissues, Surg., Gynec. & Obst. **37**:361-364 (Sept.) 1923.

Infections.—Stevens [44] reviews 113 cases of epididymitis from the Bellevue Hospital urologic service. The diagnoses were made by microscopic examination of tissue removed at operation and included seventy-four cases of genital tuberculosis, thirty-five of simple inflammation not associated with acute gonorrhea and four of syphilis. A study of the clinical, operative and pathologic records of these cases led the author to the following conclusions regarding the differential diagnosis of tuberculous and nontuberculous epididymal infections:

1. Double epididymitis slightly favors a diagnosis of tuberculosis. A prior orchidectomy or epididymectomy with inflammation ensuing in the remaining epididymis almost invariably suggests tuberculosis.

2. A scrotal sinus lasting more than one month is probably tuberculous (or possibly gummatous) in origin.

3. Tuberculosis elsewhere in the body indicates that the condition in the genital tract is also tuberculosis in over 90 per cent. of the cases.

4. Involvement of the prostate and vesicles that persists one month or longer after the development of epididymis points to tuberculosis. After six months, this becomes a marked factor in favor of tuberculosis. It is emphasized that simple inflammatory changes in the epididymis may last as long as tuberculous changes.

ANESTHESIA IN UROLOGY

Young [45] discusses the indications for various anesthetics in urologic procedures. For prostatectomy in the presence of diseased kidneys, ether is dangerous, and nitrous oxid or spinal anesthesia is preferred. In cases of high blood pressure, arteriosclerosis and cerebral disease, nitrous oxid is dangerous because it increases blood pressure. Spinal anesthesia is dangerous, since sudden marked lowering of the blood pressure may lead to cerebral thrombosis. Hence, ether with its supportive action to the heart and only slight attendant rise in blood pressure is preferable in these cases. Diabetics should receive preliminary treatment. Ether is feared in cases of tuberculosis of the genito-urinary tract because of the danger of lighting up a pulmonary focus. Nitrous oxid is desirable and carries only a slight risk in the presence of chronic infections of the mouth or respiratory tract. The importance of preliminary renal function tests is emphasized. The author concludes that ether is the anesthetic of choice in the cardiovascular cases; spinal, caudal or local procain in the tuberculous or serious renal cases; and nitrous oxid-oxygen, with as little ether as possible, in the majority of cases, and especially for patients with mild nephritis.

---

44. Stevens, A. R.: Differentiation Between Tuberculous and Nontuberculous Inflammation of the Epididymis, J. Urol. **10**:85-92 (July) 1923.

45. Young, H. H.: Choice of Anesthetic in Urology, Surg., Gynec. & Obst. **37**:109 (July) 1923.

URINARY OBSTRUCTION

Deming [46] reviews forty-eight cases collected from the literature, including one case of his own, of complete urinary obstruction due to pelvic hydatid cyst. The disease occurs most often in young and middle adult life. It occurs six times as often in the male as in the female.

Whether pelvic hydatid cysts are primary or secondary implantations from other foci, such as the liver, has been widely discussed. Most observers hold that the cysts arise in the pelvis from a hematogenous infection which localizes in the retroperitoneal cellular tissue between the bladder and rectum, but rarely in the pelvic organs themselves. However, not all cysts are found in the same tissues. Those in the ovarian and intravesical sites may be hematogenous in origin, while those in the cellular tissue between the bladder and rectum may have gained entry directly through the rectal wall. A cyst, from 8 to 20 cm. in diameter, with a wall from 2 to 5 mm. thick, composed of fibrous and muscular tissue and lined with a thin gelatinous membrane in which a large number of hooklets are found, constitutes the pathologic process. Adhesions to the rectum and bladder; torsion of the posterior urethra with consequent difficulty in catheterization, and sometimes elongation of the uterine cavity are concomitant features. The cysts are filled with a homogenous jelly-like mass in which daughter and granddaughter cysts are found. Hooklets are not difficult to demonstrate in fluid or membrane. Compression on the ureters with hydronephrosis and hydro-ureters was found in a large number of necropsies, thus explaining the uremia which not infrequently occurred as a cause of death. Rectal compression with difficult defecation was frequent. The cysts developed slowly, over a period of years. Spontaneous rupture occurred twice, once into the bladder and once into the rectum. The onset was insidious, difficulty in urination being the chief early symptom. Pain in the bladder, perineum or back was common. Gastro-intestinal symptoms were noted when infection of the liver or peritonitis was present. Loss of weight and strength occurred late. Uterine bleeding, cessation of menstruation, passage of ruptured cyst material through the rectum, sciatic pain and urticaria were occasional symptoms.

A large round tumor was many times mistaken for a distended bladder. The immobile mass, palpable liver nodules and general abdominal tenderness, and the smooth tumor, found on rectal examination to lie in the culdesac, are important aids in diagnosis. Suppuration in a cyst may occur spontaneously or, especially, from rectal puncture. This may result in rupture into the bladder, rectum, or peritoneum, in the latter case usually being followed by death.

46. Deming, C. L.: Complete Urinary Obstruction Due to Hydatid Cyst, J. Urol. **10**:1-45 (July) 1923.

Treatment is directed toward relief of urinary obstruction and disposal of the cyst. Suprapubic puncture of the cyst was uniformly fatal, and rectal puncture was usually fatal. Perineal puncture of the cyst is recommended as a method of choice for diagnosis. Marsupialization of the cyst is the best method of treatment, and incision of the cyst with suture of the wall to the edges of the abdominal wound gave good results. Seven of the forty-eight patients were not treated; twenty-five recovered; fourteen died; one developed incontinence, and one improved. The author believes that error in diagnosis was responsible for 50 per cent. of the deaths, while 40 per cent. were due to infection from suprapubic or rectal puncture. Multiple cysts usually indicate a bad prognosis.

ABSORPTION FROM THE URINARY TRACT

Magoun [47] studied the absorptive powers of the renal pelvis, ureter, bladder and urethra in dogs, using indigocarmin and phenolsulphonephthalein and *Bacillus prodigiosus,* as the materials to be absorbed. He concluded that the renal pelvis absorbs dyes and bacteria readily; the ureter and urethra absorb dyes readily, but the bacteria less readily, while the bladder absorbs a very small amount of dye and no bacteria.

These findings are of clinical importance as regards the absorption of drugs introduced into the urinary tract, and in the possibility of resorption of dyes by hydronephrotic pelves, and so forth, leading to erroneous interpretation of renal functional tests. The absorption of urine and bacteria from the posterior urethra in cases of pyelitis or of urethral inflammation is generally recognized. A number of instances of positive blood cultures in acute exacerbations of inflammation in these cases were cited.

---

47. Magoun, J. A. H., Jr.: Absorption from the Urinary Tract, J. Urol. **10**: 67-80 (July) 1923.